\mathbb{PCT}





INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7:

C12N 15/12, C07K 14/47, C12N 5/10, C07K 16/18, C12N 15/62, C12Q 1/68, G01N 33/50, 33/53, A61K 38/02, 48/00

A2 | `

(11) International Publication Number:

WO 00/37643

(43) International Publication Date:

29 June 2000 (29.06.00)

(21) International Application Number:

PCT/US99/30909

(22) International Filing Date:

23 December 1999 (23.12.99)

2.77

(30) Priority Data:

23 December 1998 (23.12.98)	US
2 July 1999 (02.07.99)	US
22 September 1999 (22.09.99)	US
19 November 1999 (19.11.99)	US
2 December 1999 (02.12.99)	US
	2 July 1999 (02.07.99) 22 September 1999 (22.09.99) 19 November 1999 (19.11.99)

(71) Applicant (for all designated States except US): CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): XU, Jiangchun [US/US]; 15805 SE 43rd Place, Bellevue, WA 98006 (US). LODES, Michael, J. [US/US]; 9223 – 36th Avenue SW, Seattle, WA 98126 (US). SECRIST, Heather [US/US]; 3844 – 35th Avenue West, Seattle, WA 98199 (US). BENSON, Darin, R. [US/US]; 723 N. 48th Street, Seattle, WA 98104 (US). MEAGHER, Madeleine, Joy [US/US]; 3819 Interlake Avenue N., Seattle, WA 98103 (US). STOLK, John [US/US]; 7436 NE 144th Place, Bothell, WA 98011

(US). WANG, Tongtong [CN/US]; 8049 NE 28th Street, Medina, WA 98039 (US). YUQIU, Jiang [CN/US]; 5001 South 232nd Street, Kent, WA 98032 (US).

(74) Agents: MAKI, David, J. et al.; Seed and Berry LLP, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY; DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as colon cancer, are disclosed. Compositions may comprise one or more colon tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a colon tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as colon cancer. Diagnostic methods based on detecting a colon tumor protein, or mRNA encoding such a protein, in a sample are also provided.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Мопасо	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IТ	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Кепуа	NL	Netherlands	YU	
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Yugoslavia Zimbabwe
Ci	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand	ZVV	Zimoaowe
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denniark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

TECHNICAL FIELD

5

10

15

20

25

30

The present invention relates generally to therapy and diagnosis of cancer, such as colon cancer. The invention is more specifically related to polypeptides comprising at least a portion of a colon tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of colon cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although advances have been made in detection and therapy of cancer, no vaccine or other universally successful method for prevention or treatment is currently available. Current therapies, which are generally based on a combination of chemotherapy or surgery and radiation, continue to prove inadequate in many patients.

Colon cancer is the second most frequently diagnosed malignancy in the United States as well as the second most common cause of cancer death. An estimated 95,600 new cases of colon cancer will be diagnosed in 1998, with an estimated 47,700 deaths. The five-year survival rate for patients with colorectal cancer detected in an early localized stage is 92%; unfortunately, only 37% of colorectal cancer is diagnosed at this stage. The survival rate drops to 64% if the cancer is allowed to spread to adjacent organs or lymph nodes, and to 7% in patients with distant metastases.

The prognosis of colon cancer is directly related to the degree of penetration of the tumor through the bowel wall and the presence or absence of nodal involvement, consequently, early detection and treatment are especially important. Currently, diagnosis is aided by the use of screening assays for fecal occult blood, sigmoidoscopy, colonoscopy and double contrast barium enemas. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. Recurrence following surgery (the most common form of therapy) is a major problem and is often the

ultimate cause of death. In spite of considerable research into therapies for the disease, colon cancer remains difficult to diagnose and treat. In spite of considerable research into therapies for these and other cancers, colon cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

5

10

15

20

25

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as colon cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a colon tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ ID NO: 1-121, 123-197 and 205-486; (b) variants of a sequence recited in SEQ ID NO: 1-121, 123-197 and 205-486; and (c) complements of a sequence of (a) or (b).

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a colon tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a colon tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polypucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under

5

10

15

20

25

conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a colon tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expresses such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be colon cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a)

5

10

15

20

25

contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached figures. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

SEQUENCE IDENTIFIERS

SEQ ID NO: 1 is a first determined cDNA sequence for Contig 1, showing homology to Neutrophil Gelatinase Associated Lipocalin.

30

5

10

15

20

15

20

SEQ ID NO: 2 is the determined cDNA sequence for Contig 2, showing no significant homology to any known genes.

SEQ ID NO: 3 is the determined cDNA sequence for Contig 4, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 4 is the determined cDNA sequence for Contig 5, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 5 is the determined cDNA sequence for Contig 9, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 6 is the determined cDNA sequence for Contig 52, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 7 is the determined cDNA sequence for Contig 6, showing homology to Villin.

SEQ ID NO: 8 is the determined cDNA sequence for Contig 8, showing no significant homology to any known genes.

SEQ ID NO: 9 is the determined cDNA sequence for Contig 10, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 10 is the determined cDNA sequence for Contig 19, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 11 is the determined cDNA sequence for Contig 21, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 12 is the determined cDNA sequence for Contig 11, showing homology to CO-029.

SEQ ID NO: 13 is the determined cDNA sequence for Contig 55, showing homology to CO-029.

SEQ ID NO: 14 is the determined cDNA sequence for Contig 12, showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P.

SEQ ID NO: 15 is the determined cDNA sequence for Contig 13, showing no significant homology to any known gene.

SEQ ID NO: 16 is the determined cDNA sequence for Contig 14, also referred to as 14261, showing no significant homology to any known gene.

10

15

20

25

30

SEQ ID NO: 17 is the determined cDNA sequence for Contig 15, showing homology to Ets-Related Transcription Factor (ERT).

SEQ ID NO: 18 is the determined cDNA sequence for Contig 16, showing homology to Chromosome 5, PAC clone 228g9 (LBNL H142).

SEQ ID NO: 19 is the determined cDNA sequence for Contig 24, showing homology to Chromosome 5, PAC clone 228g9 (LBNL H142).

SEQ ID NO: 20 is the determined cDNA sequence for Contig 17, showing homology to Cytokeratin.

SEQ ID NO: 21 is the determined cDNA sequence for Contig 18, showing homology to L1-Cadherin.

SEQ ID NO: 22 is the determined cDNA sequence for Contig 20, showing no significant homology to any known gene.

SEQ ID NO: 23 is the determined cDNA sequence for Contig 22, showing homology to Burnetanide-sensitive Na-K-Cl cotransporter (NKCCl).

SEQ ID NO: 24 is the determined cDNA sequence for Contig 23, showing no significant homology to any known gene.

SEQ ID NO: 25 is the determined cDNA sequence for Contig 25, showing homology to Macrophage Inflammatory Protein 3 alpha.

SEQ ID NO: 26 is the determined cDNA sequence for Contig 26, showing homology to Laminin.

SEQ ID NO: 27 is the determined cDNA sequence for Contig 48, showing homology to Laminin.

SEQ ID NO: 28 is the determined cDNA sequence for Contig 27, showing homology to Mytobularin (MTM1).

SEQ ID NO: 29 is the determined cDNA sequence for Contig 28, showing homology to Chromosome 16 BAC clone CIT987SK-A-363E6.

SEQ ID NO: 30 is the determined cDNA sequence for Contig 29, also referred to as C751P and 14247, showing no significant homology to any known gene, but partial homology to Rat GSK-3β-interacting protein Axil homolog.

SEQ ID NO: 31 is the determined cDNA sequence for Contig 30, showing homology to Zinc Finger Transcription Factor (ZNF207).

SEQ ID NO: 32 is the determined cDNA sequence for Contig 31, showing no significant homology to any known gene, but partial homology to Mus musculus GOB-4 homolog.

SEQ ID NO: 33 is the determined cDNA sequence for Contig 35, showing no significant homology to any known gene, but partial homology to Mus musculus GOB-4 homolog.

SEQ ID NO: 34 is the determined cDNA sequence for Contig 32, showing no significant homology to any known gene.

SEQ ID NO: 35 is the determined cDNA sequence for Contig 34, showing homology to Desmoglein 2.

SEQ ID NO: 36 is the determined cDNA sequence for Contig 36, showing no significant homology to any known gene.

SEQ ID NO: 37 is the determined cDNA sequence for Contig 37, showing homology to Putative Transmembrane Protein.

SEQ ID NO: 38 is the determined cDNA sequence for Contig 38, also referred to as C796P and 14219, showing no significant homology to any known gene.

SEQ ID NO: 39 is the determined cDNA sequence for Contig 40, showing homology to Nonspecific Cross-reacting Antigen.

SEQ ID NO: 40 is the determined cDNA sequence for Contig 41, also referred to as C799P and 14308, showing no significant homology to any known gene.

SEQ ID NO: 41 is the determined cDNA sequence for Contig 42, also referred to as C794P and 14309, showing no significant homology to any known gene.

SEQ ID NO: 42 is the determined cDNA sequence for Contig 43, showing homology to Chromosome 1 specific transcript KIAA0487.

SEQ ID NO: 43 is the determined cDNA sequence for Contig 45, showing homology to hMCM2.

SEQ ID NO: 44 is the determined cDNA sequence for Contig 46, showing homology to ETS2.

SEQ ID NO: 45 is the determined cDNA sequence for Contig 49, showing homology to Pump-1.

5

10

15

SEO ID NO: 46 is the determined cDNA sequence for Contig 50, also referred to as C792P and 18323, showing no significant homology to any known gene.

SEQ ID NO: 47 is the determined cDNA sequence for Contig 51, also referred to as C795P and 14317, showing no significant homology to any known gene.

SEQ ID NO: 48 is the determined cDNA sequence for 11092, showing no significant homology to any known gene.

SEO ID NO: 49 is the determined cDNA sequence for 11093, showing no significant homology to any known gene.

SEQ ID NO: 50 is the determined cDNA sequence for 11094, showing homology Human Putative Enterocyte Differentiation Protein.

SEQ ID NO: 51 is the determined cDNA sequence for 11095, showing homology to Human Transcriptional Corepressor hKAP1/TIF1B mRNA.

SEQ ID NO: 52 is the determined cDNA sequence for 11096, showing no significant homology to any known gene.

SEO ID NO: 53 is the determined cDNA sequence for 11097, showing homology to Human Nonspecific Antigen.

SEQ ID NO: 54 is the determined cDNA sequence for 11098, showing no significant homology to any known gene.

SEO ID NO: 55 is the determined cDNA sequence for 11099, showing homology to Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEO ID NO: 56 is the determined cDNA sequence for 11186, showing homology to Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEO ID NO: 57 is the determined cDNA sequence for 11101, showing homology to Human Chromosome X.

SEO ID NO: 58 is the determined cDNA sequence for 11102, showing homology to Human Chromosome X.

SEQ ID NO: 59 is the determined cDNA sequence for 11103, showing no significant homology to any known gene.

SEQ ID NO: 60 is the determined cDNA sequence for 11174, showing no significant homology to any known gene. 30

5

10

15

20



SEQ ID NO: 61 is the determined cDNA sequence for 11104, showing homology to Human mRNA for KIAA0154.

SEQ ID NO: 62 is the determined cDNA sequence for 11105, showing homology toHuman Apurinic/Apyrimidinic Endonuclease (hap1)mRNA.

SEQ ID NO: 63 is the determined cDNA sequence for 11106, showing homology toHuman Chromosome 12p13.

SEQ ID NO: 64 is the determined cDNA sequence for 11107, showing homology to Human 90 kDa Heat Shock Protein.

SEQ ID NO: 65 is the determined cDNA sequence for 11108, showing no significant 10. homology-to-any-known-gene.

SEQ ID NO: 66 is the determined cDNA sequence for 11112, showing no significant homology to any known gene.

SEQ ID NO: 67 is the determined cDNA sequence for 11115, showing no significant homology to any known gene.

SEQ ID NO: 68 is the determined cDNA sequence for 11117, showing no significant 15 homology to any known gene.

SEQ ID NO: 69 is the determined cDNA sequence for 11118, showing no significant homology to any known gene.

SEQ ID NO: 70 is the determined cDNA sequence for 11119, showing homology to Human Elongation Factor 1-alpha. 20

SEQ ID NO: 71 is the determined cDNA sequence for 11121, showing homology to Human Lamin B Receptor (LBR) mRNA.

SEQ ID NO: 72 is the determined cDNA sequence for 11122, showing homology to H. sapiens mRNA for Novel Glucocorticoid.

SEQ ID NO: 73 is the determined cDNA sequence for 11123, showing homology to 25 H. sapiens mRNA for snRNP protein B.

SEQ ID NO: 74 is the determined cDNA sequence for 11124, showing homology to Human Cisplatin Resistance Associated Beta-protein.

SEQ ID NO: 75 is the determined cDNA sequence for 11127, showing homology to M. musculus Calumenin mRNA. 30

15

20

25



SEQ ID NO: 76 is the determined cDNA sequence for 11128, showing homology to Human ras-related small GTP binding protein.

SEQ ID NO: 77 is the determined cDNA sequence for 11130, showing homology to Human Cosmid U169d2.

SEQ ID NO: 78 is the determined cDNA sequence for 11131, showing homology to H. sapiens mRNA for protein homologous to Elongation 1-g.

SEQ ID NO: 79 is the determined cDNA sequence for 11134, showing no significant homology to any known gene.

SEQ ID NO: 80 is the determined cDNA sequence for 11135, showing homology to H. sapiens Nieman-Pick (NPC1) mRNA.

SEQ ID NO: 81 is the determined cDNA sequence for 11137, showing homology to H. sapiens mRNA for Niecin b-chain.

SEQ ID NO: 82 is the determined cDNA sequence for 11138, showing homology to Human Endogenous Retroviral Protease mRNA.

SEQ ID NO: 83 is the determined cDNA sequence for 11139, showing homology to H. sapiens mRNA for DMBT1 protein.

SEQ ID NO: 84 is the determined cDNA sequence for 11140, showing homology to H. sapiens ras GTPase activating-like protein.

SEQ ID NO: 85 is the determined cDNA sequence for 11143, showing homology to Human Acidic Ribosomal Phosphoprotein PO mRNA.

SEQ ID NO: 86 is the determined cDNA sequence for 11144, showing homology to H. sapiens U21 mRNA.

SEQ ID NO: 87 is the determined cDNA sequence for 11145, showing homology to Human GTP-binding protein.

SEQ ID NO: 88 is the determined cDNA sequence for 11148, showing homology to H. sapiens U21 mRNA.

SEQ ID NO: 89 is the determined cDNA sequence for 11151, showing no significant homology to any known gene.

SEQ ID NO: 90 is the determined cDNA sequence for 11154, showing no significant homology to any known gene.

20



SEQ ID NO: 91 is the determined cDNA sequence for 11156, showing homology to H. sapiens Ribosomal Protein L27.

SEQ ID NO: 92 is the determined cDNA sequence for 11157, showing homology to H. sapiens Ribosomal Protein L27.

SEQ ID NO: 93 is the determined cDNA sequence for 11158, showing no significant homology to any known gene.

SEQ ID NO: 94 is the determined cDNA sequence for 11162, showing homology to Ag-X antigen.

SEQ ID NO: 95 is the determined cDNA sequence for 11164, showing homology to H. sapiens mRNA for Signal Recognition Protein sub14.

SEQ ID NO: 96 is the determined cDNA sequence for 11165, showing homology to Human PAC 204e5/127h14.

SEQ ID NO: 97 is the determined cDNA sequence for 11166, showing homology to Human mRNA for KIAA0108.

SEQ ID NO: 98 is the determined cDNA sequence for 11167, showing homology to H. sapiens mRNA for Neutrophil Gelatinase asset. Lipocalin.

SEQ ID NO: 99 is the determined cDNA sequence for 11168, showing no significant homology to any known gene.

SEQ ID NO: 100 is the determined cDNA sequence for 11172, showing no significant homology to any known gene.

SEQ ID NO: 101 is the determined cDNA sequence for 11175, showing no significant homology to any known gene.

SEQ ID NO: 102 is the determined cDNA sequence for 11176, showing homology to Human maspin mRNA.

SEQ ID NO: 103 is the determined cDNA sequence for 11177, showing homology to Human Carcinoembryonic Antigen.

SEQ ID NO: 104 is the determined cDNA sequence for 11178, showing homology to Human A-Tubulin mRNA.

SEQ ID NO: 105 is the determined cDNA sequence for 11179, showing homology to Human mRNA for proton-ATPase-like protein.

10

15

20

25

SEQ ID NO: 106 is the determined cDNA sequence for 11180, showing homology to Human HepG2 3' region cDNA clone hmd.

SEQ ID NO: 107 is the determined cDNA sequence for 11182, showing homology to Human MHC homologous to Chicken B-Complex Protein.

SEQ ID NO: 108 is the determined cDNA sequence for 11183, showing homology to Human High Mobility Group Box (SSRP1) mRNA.

SEQ ID NO: 109 is the determined cDNA sequence for 11184, showing no significant homology to any known gene.

SEQ ID NO: 110 is the determined cDNA sequence for 11185, showing no significant homology to any known gene.

SEQ ID NO: 111 is the determined cDNA sequence for 11187, showing no significant homology to any known gene.

SEQ ID NO: 112 is the determined cDNA sequence for 11190, showing homology to Human Replication Protein A 70kDa.

SEQ ID NO: 113 is the determined cDNA sequence for Contig 47, also referred to as C797P, showing homology to Human Chromosome X clone bWXD342.

SEQ ID NO: 114 is the determined cDNA sequence for Contig 7, showing homology to Equilibrative Nucleoside Transporter 2 (ent2).

SEQ ID NO: 115 is the determined cDNA sequence for 14235.1, also referred to as C791P, showing homology to H. sapiens chromosome 21 derived BAC containing ets-2 gene.

SEQ ID NO: 116 is the determined cDNA sequence for 14287.2, showing no significant homology to any known gene, but some degree of homology to Putative Transmembrane Protein.

SEQ ID NO: 117 is the determined cDNA sequence for 14233.1, also referred to as Contig 48, showing no significant homology to any known gene.

SEQ ID NO: 118 is the determined cDNA sequence for 14298.2, also referred to as C793P, showing no significant homology to any known gene.

SEQ ID NO: 119 is the determined cDNA sequence for 14372, also referred to as
Contig 44, showing no significant homology to any known gene.

15

20

25



SEQ ID NO: 120 is the determined cDNA sequence for 14295, showing homology to secreted cement gland protein XAG-2 homolog.

SEQ ID NO: 121 is the determined full-length cDNA sequence for a clone showing homology to Beta IG-H3.

SEQ ID NO: 122 is the predicted amino acid sequence for the clone of SEQ ID NO: 121.

SEQ ID NO: 123 is a longer determined cDNA sequence for C751P.

SEQ ID NO: 124 is a longer determined cDNA sequence for C791P.

SEQ ID NO: 125 is a longer determined cDNA sequence for C792P.

SEQ ID NO: 126 is a longer determined cDNA sequence for C793P.

SEQ ID NO: 127 is a longer determined cDNA sequence for C794P.

SEQ ID NO: 128 is a longer determined cDNA sequence for C795P.

SEQ ID NO: 129 is a longer determined cDNA sequence for C796P.

SEQ ID NO: 130 is a longer determined cDNA sequence for C797P.

SEQ ID NO: 131 is a longer determined cDNA sequence for C798P.

SEQ ID NO: 132 is a longer determined cDNA sequence for C799P.

SEQ ID NO: 133 is a first partial determined cDNA sequence for CoSub-3 (also known as 23569).

SEQ ID NO: 134 is a second partial determined cDNA sequence for CoSub-3 (also known as 23569).

SEQ ID NO: 135 is a first partial determined cDNA sequence for CoSub-13 (also known as 23579).

SEQ ID NO: 136 is a second partial determined cDNA sequence for CoSub-13 (also known as 23579).

SEQ ID NO: 137 is the determined cDNA sequence for CoSub-17 (also known as 23583).

SEQ ID NO: 138 is the determined cDNA sequence for CoSub-19 (also known as 23585).

SEQ ID NO: 139 is the determined cDNA sequence for CoSub-22 (also known as 23714).

- SEQ ID NO: 140 is the determined cDNA sequence for CoSub-23 (also known as 23715).
- SEQ ID NO: 141 is the determined cDNA sequence for CoSub-26 (also known as 23717).
- SEQ ID NO: 142 is the determined cDNA sequence for CoSub-33 (also known as 23724).
 - SEQ ID NO: 143 is the determined cDNA sequence for CoSub-34 (also known as 23725).
- SEQ ID NO: 144 is the determined cDNA sequence for CoSub-35 (also known as 23726).
 - SEQ ID NO: 145 is the determined cDNA sequence for CoSub-37 (also known as 23728).
 - SEQ ID NO: 146 is the determined cDNA sequence for CoSub-39 (also known as 23730).
- SEQ ID NO: 147 is the determined cDNA sequence for CoSub-42 (also known as 23766).
 - SEQ ID NO: 148 is the determined cDNA sequence for CoSub-44 (also known as 23768).
- SEQ ID NO: 149 is the determined cDNA sequence for CoSub-47 (also known as 23771).
 - SEQ ID NO: 150 is the determined cDNA sequence for CoSub-54 (also known as 23778).
 - SEQ ID NO: 151 is the determined cDNA sequence for CoSub-55 (also known as 23779).
- SEQ ID NO: 152 is the determined cDNA sequence for CT1 (also known as 24099).
 - SEQ ID NO: 153 is the determined cDNA sequence for CT2 (also known as 24100).
 - SEQ ID NO: 154 is the determined cDNA sequence for CT3 (also known as 24101).
 - SEQ ID NO: 155 is the determined cDNA sequence for CT6 (also known as 24104).
 - SEO ID NO: 156 is the determined cDNA sequence for CT7 (also known as 24105).
- SEQ ID NO: 157 is the determined cDNA sequence for CT12 (also known as 24110).
 - SEO ID NO: 158 is the determined cDNA sequence for CT13 (also known as 24111).

15



SEQ ID NO: 159 is the determined cDNA sequence for CT14 (also known as 24112).

SEQ ID NO: 160 is the determined cDNA sequence for CT15 (also known as 24113).

SEQ ID NO: 161 is the determined cDNA sequence for CT17 (also known as 24115).

SEQ ID NO: 162 is the determined cDNA sequence for CT18 (also known as 24116).

SEQ ID NO: 163 is the determined cDNA sequence for CT22 (also known as 23848).

SEQ ID NO: 164 is the determined cDNA sequence for CT24 (also known as 23849).

SEQ ID NO: 165 is the determined cDNA sequence for CT31 (also known as 23854).

SEQ ID NO: 166 is the determined cDNA sequence for CT34 (also known as 23856).

SEQ ID NO: 167 is the determined cDNA sequence for CT37 (also known as 23859).

SEQ-ID-NO: 168 is the determined cDNA sequence for CT39 (also known as 23860).

SEQ ID NO: 169 is the determined cDNA sequence for CT40 (also known as 23861).

SEQ ID NO: 170 is the determined cDNA sequence for CT51 (also known as 24130).

SEQ ID NO: 171 is the determined cDNA sequence for CT53 (also known as 24132).

SEQ ID NO: 172 is the determined cDNA sequence for CT63 (also known as 24595).

SEQ ID NO: 173 is the determined cDNA sequence for CT88 (also known as 24608).

SEQ ID NO: 174 is the determined cDNA sequence for CT92 (also known as 24800).

SEQ ID NO: 175 is the determined cDNA sequence for CT94 (also known as 24802).

SEQ ID NO: 176 is the determined cDNA sequence for CT102 (also known as 24805).

SEQ ID NO: 177 is the determined cDNA sequence for CT103 (also known as 24806).

SEQ ID NO: 178 is the determined cDNA sequence for CT111 (also known as 25520).

SEQ ID NO: 179 is the determined cDNA sequence for CT118 (also known as 25 25522).

SEQ ID NO: 180 is the determined cDNA sequence for CT121 (also known as 25523).

SEQ ID NO: 181 is the determined cDNA sequence for CT126 (also known as 25527).

SEQ ID NO: 182 is the determined cDNA sequence for CT135 (also known as 25534).

- SEQ ID NO: 183 is the determined cDNA sequence for CT140 (also known as 25537).
- SEQ ID NO: 184 is the determined cDNA sequence for CT145 (also known as 25542).
- SEQ ID NO: 185 is the determined cDNA sequence for CT147 (also known as 25543).
 - SEQ ID NO: 186 is the determined cDNA sequence for CT148 (also known as 25544).
- SEQ ID NO: 187 is the determined cDNA sequence for CT502 (also known as 26420).
 - SEQ ID NO: 188 is the determined cDNA sequence for CT507 (also known as 26425).
 - SEQ ID NO: 189 is the determined cDNA sequence for CT521 (also known as 27366).
- SEQ ID NO: 190 is the determined cDNA sequence for CT544 (also known as 27375).
 - SEQ ID NO: 191 is the determined cDNA sequence for CT577 (also known as 27385).
- SEQ ID NO: 192 is the determined cDNA sequence for CT580 (also known as 20 27387).
 - SEQ ID NO: 193 is the determined cDNA sequence for CT594 (also known as 27540).
 - SEQ ID NO: 194 is the determined cDNA sequence for CT606 (also known as 27547).
- SEQ ID NO: 195 is the determined cDNA sequence for CT607 (also known as 27548).
 - SEQ ID NO: 196 is the determined cDNA sequence for CT599 (also known as 27903).
- SEQ ID NO: 197 is the determined cDNA sequence for CT632 (also known as 27922).
 - SEQ ID NO: 198 is the predicted amino acid sequence for CT502 (SEQ ID NO: 187).

SEQ ID NO: 199 is the predicted amino acid sequence for CT507 (SEQ ID NO: 188). SEQ ID NO: 200 is the predicted amino acid sequence for CT521 (SEQ ID NO: 189). SEQ ID NO: 201 is the predicted amino acid sequence for CT544 (SEQ ID NO: 190). SEQ ID NO: 202 is the predicted amino acid sequence for CT606 (SEQ ID NO: 194). SEQ ID NO: 203 is the predicted amino acid sequence for CT607 (SEQ ID NO: 195). 5 SEQ ID NO: 204 is the predicted amino acid sequence for CT632 (SEQ ID NO: 197). SEQ ID NO: 205 is the determined cDNA sequence for clone 25244. SEQ ID NO: 206 is the determined cDNA sequence for clone 25245. SEQ ID NO: 207 is the determined cDNA sequence for clone 25246. SEQ ID NO: 208 is the determined cDNA sequence for clone 25248. 10 SEQ ID NO: 209 is the determined cDNA sequence for clone 25249. SEQ ID NO: 210 is the determined cDNA sequence for clone 25250. SEQ ID NO: 211 is the determined cDNA sequence for clone 25251. SEQ ID NO: 212 is the determined cDNA sequence for clone 25252. SEQ ID NO: 213 is the determined cDNA sequence for clone 25253. 15 SEQ ID NO: 214 is the determined cDNA sequence for clone 25254. SEQ ID NO: 215 is the determined cDNA sequence for clone 25255. SEQ ID NO: 216 is the determined cDNA sequence for clone 25256. SEQ ID NO: 217 is the determined cDNA sequence for clone 25257. 20 SEQ ID NO: 218 is the determined cDNA sequence for clone 25259. SEQ ID NO: 219 is the determined cDNA sequence for clone 25260. SEQ ID NO: 220 is the determined cDNA sequence for clone 25261. SEQ ID NO: 221 is the determined cDNA sequence for clone 25262. SEQ ID NO: 222 is the determined cDNA sequence for clone 25263. SEQ ID NO: 223 is the determined cDNA sequence for clone 25264. 25 SEQ ID NO: 224 is the determined cDNA sequence for clone 25265. SEQ ID NO: 225 is the determined cDNA sequence for clone 25266. SEQ ID NO: 226 is the determined cDNA sequence for clone 25267. SEQ ID NO: 227 is the determined cDNA sequence for clone 25268. 30 SEQ ID NO: 228 is the determined cDNA sequence for clone 25269. SEQ ID NO: 229 is the determined cDNA sequence for clone 25271.

	SEQ ID NO: 230 is the determined cDNA sequence for clone 25272.
	SEQ ID NO: 231 is the determined cDNA sequence for clone 25273.
	SEQ ID NO: 232 is the determined cDNA sequence for clone 25274.
	SEQ ID NO: 233 is the determined cDNA sequence for clone 25275.
5	SEQ ID NO: 234 is the determined cDNA sequence for clone 25276.
	SEQ ID NO: 235 is the determined cDNA sequence for clone 25277.
	SEQ ID NO: 236 is the determined cDNA sequence for clone 25278.
	SEQ ID NO: 237 is the determined cDNA sequence for clone 25280.
	SEQ ID NO: 238 is the determined cDNA sequence for clone 25281.
10	SEQ ID NO: 239 is the determined cDNA sequence for clone 25282.
	SEQ ID NO: 240 is the determined cDNA sequence for clone 25283.
	SEQ ID NO: 241 is the determined cDNA sequence for clone 25284.
	SEQ ID NO: 242 is the determined cDNA sequence for clone 25285.
	SEQ ID NO: 243 is the determined cDNA sequence for clone 25286.
15	SEQ ID NO: 244 is the determined cDNA sequence for clone 25287.
	SEQ ID NO: 245 is the determined cDNA sequence for clone 25288.
	SEQ ID NO: 246 is the determined cDNA sequence for clone 25289.
	SEQ ID NO: 247 is the determined cDNA sequence for clone 25290.
	SEQ ID NO: 248 is the determined cDNA sequence for clone 25291.
20	SEQ ID NO: 249 is the determined cDNA sequence for clone 25292.
	SEQ ID NO: 250 is the determined cDNA sequence for clone 25293.
	SEQ ID NO: 251 is the determined cDNA sequence for clone 25294.
	SEQ ID NO: 252 is the determined cDNA sequence for clone 25295.
	SEQ ID NO: 253 is the determined cDNA sequence for clone 25296.
25	SEQ ID NO: 254 is the determined cDNA sequence for clone 25297.
	SEQ ID NO: 255 is the determined cDNA sequence for clone 25418.
	SEQ ID NO: 256 is the determined cDNA sequence for clone 25419.
	SEQ ID NO: 257 is the determined cDNA sequence for clone 25420.
	SEQ ID NO: 258 is the determined cDNA sequence for clone 25421.
30	SEQ ID NO: 259 is the determined cDNA sequence for clone 25422.

SEQ ID NO: 260 is the determined cDNA sequence for clone 25423.

	SEQ ID NO: 261 is the determined cDNA sequence for clone 25424.
	SEQ ID NO: 262 is the determined cDNA sequence for clone 25426.
	SEQ ID NO: 263 is the determined cDNA sequence for clone 25427.
	SEQ ID NO: 264 is the determined cDNA sequence for clone 25428.
5	SEQ ID NO: 265 is the determined cDNA sequence for clone 25429.
	SEQ ID NO: 266 is the determined cDNA sequence for clone 25430.
	SEQ ID NO: 267 is the determined cDNA sequence for clone 25431.
	SEQ ID NO: 268 is the determined cDNA sequence for clone 25432.
	SEQ ID NO: 269 is the determined cDNA sequence for clone 25433.
10	SEQ ID NO: 270 is the determined cDNA sequence for clone 25434.
	SEQ ID NO: 271 is the determined cDNA sequence for clone 25435.
	SEQ ID NO: 272 is the determined cDNA sequence for clone 25436.
	SEQ ID NO: 273 is the determined cDNA sequence for clone 25437.
	SEQ ID NO: 274 is the determined cDNA sequence for clone 25438.
15	SEQ ID NO: 275 is the determined cDNA sequence for clone 25439.
	SEQ ID NO: 276 is the determined cDNA sequence for clone 25440.
	SEQ ID NO: 277 is the determined cDNA sequence for clone 25441.
	SEQ ID NO: 278 is the determined cDNA sequence for clone 25442.
	SEQ ID NO: 279 is the determined cDNA sequence for clone 25443.
20	SEQ ID NO: 280 is the determined cDNA sequence for clone 25444.
	SEQ ID NO: 281 is the determined cDNA sequence for clone 25445.
	SEQ ID NO: 282 is the determined cDNA sequence for clone 25446.
	SEQ ID NO: 283 is the determined cDNA sequence for clone 25447.
	SEQ ID NO: 284 is the determined cDNA sequence for clone 25448.
25	SEQ ID NO: 285 is the determined cDNA sequence for clone 25844.
	SEQ ID NO: 286 is the determined cDNA sequence for clone 25845.
	SEQ ID NO: 287 is the determined cDNA sequence for clone 25846.
	SEQ ID NO: 288 is the determined cDNA sequence for clone 25847.
	SEQ ID NO: 289 is the determined cDNA sequence for clone 25848.
30	SEQ ID NO: 290 is the determined cDNA sequence for clone 25850.
	SEQ ID NO: 291 is the determined cDNA sequence for clone 25851.

SEQ ID NO: 292 is the determined cDNA sequence for clone 25852. SEO ID NO: 293 is the determined cDNA sequence for clone 25853. SEQ ID NO: 294 is the determined cDNA sequence for clone 25854. SEQ ID NO: 295 is the determined cDNA sequence for clone 25855. SEO ID NO: 296 is the determined cDNA sequence for clone 25856. 5 SEO ID NO: 297 is the determined cDNA sequence for clone 25857. SEQ ID NO: 298 is the determined cDNA sequence for clone 25858. SEQ ID NO: 299 is the determined cDNA sequence for clone 25859. SEO ID NO: 300 is the determined cDNA sequence for clone 25860. SEQ ID NO: 301 is the determined cDNA sequence for clone 25861. 10 SEQ ID NO: 302 is the determined cDNA sequence for clone 25862. SEQ ID NO: 303 is the determined cDNA sequence for clone 25863. SEQ ID NO: 304 is the determined cDNA sequence for clone 25864. SEQ ID NO: 305 is the determined cDNA sequence for clone 25865. SEQ ID NO: 306 is the determined cDNA sequence for clone 25866. 15 SEO ID NO: 307 is the determined cDNA sequence for clone 25867. SEQ ID NO: 308 is the determined cDNA sequence for clone 25868. SEQ ID NO: 309 is the determined cDNA sequence for clone 25869. SEQ ID NO: 310 is the determined cDNA sequence for clone 25870. SEQ ID NO: 311 is the determined cDNA sequence for clone 25871. 20 SEQ ID NO: 312 is the determined cDNA sequence for clone 25872. SEQ ID NO: 313 is the determined cDNA sequence for clone 25873. SEQ ID NO: 314 is the determined cDNA sequence for clone 25875. SEQ ID NO: 315 is the determined cDNA sequence for clone 25876. SEQ ID NO: 316 is the determined cDNA sequence for clone 25877. 25 SEQ ID NO: 317 is the determined cDNA sequence for clone 25878. SEO ID NO: 318 is the determined cDNA sequence for clone 25879. SEQ ID NO: 319 is the determined cDNA sequence for clone 25880. SEQ ID NO: 320 is the determined cDNA sequence for clone 25881. SEQ ID NO: 321 is the determined cDNA sequence for clone 25882. 30 SEO ID NO: 322 is the determined cDNA sequence for clone 25883. WO 00/37643

22

PCT/US99/30909

SEQ ID NO: 323 is the determined cDNA sequence for clone 25884. SEQ ID NO: 324 is the determined cDNA sequence for clone 25885. SEQ ID NO: 325 is the determined cDNA sequence for clone 25886. SEQ ID NO: 326 is the determined cDNA sequence for clone 25887. SEQ ID NO: 327 is the determined cDNA sequence for clone 25888. 5 SEQ ID NO: 328 is the determined cDNA sequence for clone 25889. SEQ ID NO: 329 is the determined cDNA sequence for clone 25890. SEQ ID NO: 330 is the determined cDNA sequence for clone 25892. SEQ ID NO: 331 is the determined cDNA sequence for clone 25894. SEQ ID NO: 332 is the determined cDNA sequence for clone 25895. 10 SEQ ID NO: 333 is the determined cDNA sequence for clone 25896. SEQ ID NO: 334 is the determined cDNA sequence for clone 25897. SEQ ID NO: 335 is the determined cDNA sequence for clone 25899. SEQ ID NO: 336 is the determined cDNA sequence for clone 25900. SEQ ID NO: 337 is the determined cDNA sequence for clone 25901. 15 SEQ ID NO: 338 is the determined cDNA sequence for clone 25902. SEQ ID NO: 339 is the determined cDNA sequence for clone 25903. SEQ ID NO: 340 is the determined cDNA sequence for clone 25904. SEQ ID NO: 341 is the determined cDNA sequence for clone 25906. SEQ ID NO: 342 is the determined cDNA sequence for clone 25907. 20 SEQ ID NO: 343 is the determined cDNA sequence for clone 25908. SEQ ID NO: 344 is the determined cDNA sequence for clone 25909. SEQ ID NO: 345 is the determined cDNA sequence for clone 25910. SEQ ID NO: 346 is the determined cDNA sequence for clone 25911. SEQ ID NO: 347 is the determined cDNA sequence for clone 25912. 25 SEQ ID NO: 348 is the determined cDNA sequence for clone 25913. SEQ ID NO: 349 is the determined cDNA sequence for clone 25914. SEQ ID NO: 350 is the determined cDNA sequence for clone 25915. SEQ ID NO: 351 is the determined cDNA sequence for clone 25916. SEQ ID NO: 352 is the determined cDNA sequence for clone 25917. 30 SEQ ID NO: 353 is the determined cDNA sequence for clone 25918.

SEO ID NO: 354 is the determined cDNA sequence for clone 25919. SEQ ID NO: 355 is the determined cDNA sequence for clone 25920. SEQ ID NO: 356 is the determined cDNA sequence for clone 25921. SEQ ID NO: 357 is the determined cDNA sequence for clone 25922. SEQ ID NO: 358 is the determined cDNA sequence for clone 25924. SEQ ID NO: 359 is the determined cDNA sequence for clone 25925. SEQ ID NO: 360 is the determined cDNA sequence for clone 25926. SEQ ID NO: 361 is the determined cDNA sequence for clone 25927. SEQ ID NO: 362 is the determined cDNA sequence for clone 25928. SEQ ID NO: 363 is the determined cDNA sequence for clone 25929. SEO ID NO: 364 is the determined cDNA sequence for clone 25930. SEQ ID NO: 365 is the determined cDNA sequence for clone 25931. SEQ ID NO: 366 is the determined cDNA sequence for clone 25932. SEO ID NO: 367 is the determined cDNA sequence for clone 25933. SEO ID NO: 368 is the determined cDNA sequence for clone 25934. SEQ ID NO: 369 is the determined cDNA sequence for clone 25935. SEO ID NO: 370 is the determined cDNA sequence for clone 25936. SEO ID NO: 371 is the determined cDNA sequence for clone 25939. SEQ ID NO: 372 is the determined cDNA sequence for clone 32016. SEQ ID NO: 373 is the determined cDNA sequence for clone 32021. SEQ ID NO: 374 is the determined cDNA sequence for clone 31993. SEO ID NO: 375 is the determined cDNA sequence for clone 31997. SEQ ID NO: 376 is the determined cDNA sequence for clone 31942. SEQ ID NO: 377 is the determined cDNA sequence for clone 31937.

23

SEQ ID NO: 380 is the determined cDNA sequence for clone 31961.

SEQ ID NO: 381 is the determined cDNA sequence for clone 31964.

SEQ ID NO: 382 is the determined cDNA sequence for clone 32005.

SEQ ID NO: 383 is the determined cDNA sequence for clone 31980.

SEQ ID NO: 384 is the determined cDNA sequence for clone 31940.

SEO ID NO: 378 is the determined cDNA sequence for clone 31952.

SEQ ID NO: 379 is the determined cDNA sequence for clone 31992.

5

10

15

20

SEQ ID NO: 385 is the determined cDNA sequence for clone 32004. SEQ ID NO: 386 is the determined cDNA sequence for clone 31956. SEQ ID NO: 387 is the determined cDNA sequence for clone 31934. SEQ ID NO: 388 is the determined cDNA sequence for clone 31998. SEQ ID NO: 389 is the determined cDNA sequence for clone 31973. 5 SEQ ID NO: 390 is the determined cDNA sequence for clone 31976. SEQ ID NO: 391 is the determined cDNA sequence for clone 31988. SEQ ID NO: 392 is the determined cDNA sequence for clone 31948. SEQ ID NO: 393 is the determined cDNA sequence for clone 32013. SEQ ID NO: 394 is the determined cDNA sequence for clone 31986. 10 SEQ ID NO: 395 is the determined cDNA sequence for clone 31954. SEQ ID NO: 396 is the determined cDNA sequence for clone 31987. SEQ ID NO: 397 is the determined cDNA sequence for clone 32029. SEQ ID NO: 398 is the determined cDNA sequence for clone 32028. SEQ ID NO: 399 is the determined cDNA sequence for clone 32012. 15 SEQ ID NO: 400 is the determined cDNA sequence for clone 31959. SEQ ID NO: 401 is the determined cDNA sequence for clone 32027. SEQ ID NO: 402 is the determined cDNA sequence for clone 31957. SEQ ID NO: 403 is the determined cDNA sequence for clone 31950. SEQ ID NO: 404 is the determined cDNA sequence for clone 32011. 20 SEQ ID NO: 405 is the determined cDNA sequence for clone 32022. SEQ ID NO: 406 is the determined cDNA sequence for clone 32014. SEQ ID NO: 407 is the determined cDNA sequence for clone 31963. SEQ ID NO: 408 is the determined cDNA sequence for clone 31989. SEQ ID NO: 409 is the determined cDNA sequence for clone 32015. 25 SEQ ID NO: 410 is the determined cDNA sequence for clone 32002. SEQ ID NO: 411 is the determined cDNA sequence for clone 31939. SEQ ID NO: 412 is the determined cDNA sequence for clone 32003. SEQ ID NO: 413 is the determined cDNA sequence for clone 31936. SEQ ID NO: 414 is the determined cDNA sequence for clone 32007. 30 SEQ ID NO: 415 is the determined cDNA sequence for clone 31965.



SEQ ID NO: 416 is the determined cDNA sequence for clone 31935. SEQ ID NO: 417 is the determined cDNA sequence for clone 32008. SEQ ID NO: 418 is the determined cDNA sequence for clone 31966. SEQ ID NO: 419 is the determined cDNA sequence for clone 32020. SEQ ID NO: 420 is the determined cDNA sequence for clone 31971. 5 SEQ ID NO: 421 is the determined cDNA sequence for clone 31977. SEQ ID NO: 422 is the determined cDNA sequence for clone 31985. SEQ ID NO: 423 is the determined cDNA sequence for clone 32023. SEQ ID NO: 424 is the determined cDNA sequence for clone 31981. 10 SEQ ID NO: 425 is the determined cDNA sequence for clone 32006. SEQ ID NO: 426 is the determined cDNA sequence for clone 31991. SEQ ID NO: 427 is the determined cDNA sequence for clone 31995. SEQ ID NO: 428 is the determined cDNA sequence for clone 32000. SEQ ID NO: 429 is the determined cDNA sequence for clone 31990. 15 SEQ ID NO: 430 is the determined cDNA sequence for clone 31946. SEQ ID NO: 431 is the determined cDNA sequence for clone 31938. SEQ ID NO: 432 is the determined cDNA sequence for clone 31941. SEQ ID NO: 433 is the determined cDNA sequence for clone 31982. SEQ ID NO: 434 is the determined cDNA sequence for clone 31996. SEQ ID NO: 435 is the determined cDNA sequence for clone 32010. 20 SEQ ID NO: 436 is the determined cDNA sequence for clone 31974. SEQ ID NO: 437 is the determined cDNA sequence for clone 31983. SEQ ID NO: 438 is the determined cDNA sequence for clone 31999. SEQ ID NO: 439 is the determined cDNA sequence for clone 31949. 25 SEQ ID NO: 440 is the determined cDNA sequence for clone 31947. SEQ ID NO: 441 is the determined cDNA sequence for clone 31994. SEQ ID NO: 442 is the determined cDNA sequence for clone 31958. SEQ ID NO: 443 is the determined cDNA sequence for clone 31975. SEQ ID NO: 444 is the determined cDNA sequence for clone 31984. SEQ ID NO: 445 is the determined cDNA sequence for clone 32024. 30 SEQ ID NO: 446 is the determined cDNA sequence for clone 31972.

SEQ ID NO: 447 is the determined cDNA sequence for clone 31943. SEQ ID NO: 448 is the determined cDNA sequence for clone 32018. SEQ ID NO: 449 is the determined cDNA sequence for clone 32026. SEQ ID NO: 450 is the determined cDNA sequence for clone 32009. 5 SEQ ID NO: 451 is the determined cDNA sequence for clone 32019. SEQ ID NO: 452 is the determined cDNA sequence for clone 32025. SEQ ID NO: 453 is the determined cDNA sequence for clone 31967. SEQ ID NO: 454 is the determined cDNA sequence for clone 31968. SEQ ID NO: 455 is the determined cDNA sequence for clone 31955. SEQ ID NO: 456 is the determined cDNA sequence for clone 31951. SEQ ID NO: 457 is the determined cDNA sequence for clone 31970. SEQ ID NO: 458 is the determined cDNA sequence for clone 31962. SEQ ID NO: 459 is the determined cDNA sequence for clone 32001. SEQ ID NO: 460 is the determined cDNA sequence for clone 31953. SEQ ID NO: 461 is the determined cDNA sequence for clone 31944. 15 SEQ ID NO: 462 is the determined cDNA sequence for clone 31825. SEQ ID NO: 463 is the determined cDNA sequence for clone 31828. SEQ ID NO: 464 is the determined cDNA sequence for clone 31830. SEQ ID NO: 465 is the determined cDNA sequence for clone 31841. 20 SEQ ID NO: 466 is the determined cDNA sequence for clone 31847. SEQ ID NO: 467 is the determined cDNA sequence for clone 31850. SEQ ID NO: 468 is the determined cDNA sequence for clone 31852. SEQ ID NO: 469 is the determined cDNA sequence for clone 31855. SEQ ID NO: 470 is the determined cDNA sequence for clone 31858. 25 SEQ ID NO: 471 is the determined cDNA sequence for clone 31861. SEQ ID NO: 472 is the determined cDNA sequence for clone 31868. SEQ ID NO: 473 is the determined cDNA sequence for clone 31870. SEQ ID NO: 474 is the determined cDNA sequence for clone 31872. SEQ ID NO: 475 is the determined cDNA sequence for clone 31873. 30 SEQ ID NO: 476 is the determined cDNA sequence for clone 31877. SEQ ID NO: 477 is the determined cDNA sequence for clone 31878.

SEQ ID NO: 478 is the determined cDNA sequence for clone 31885.

SEQ ID NO: 479 is the determined cDNA sequence for clone 31888.

SEQ ID NO: 480 is the determined cDNA sequence for clone 31890.

SEQ ID NO: 481 is the determined cDNA sequence for clone 31893.

SEQ ID NO: 482 is the determined cDNA sequence for clone 31898.

SEQ ID NO: 483 is the determined cDNA sequence for clone 31901.

SEQ ID NO: 484 is the determined cDNA sequence for clone 31909.

SEQ ID NO: 485 is the determined cDNA sequence for clone 31910.

SEQ ID NO: 486 is the determined cDNA sequence for clone 31914.

10

15

20

25

5

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as colon cancer. The compositions described herein may include colon tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a colon tumor protein or a variant thereof. A "colon tumor protein" is a protein that is expressed in colon tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain colon tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with colon cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human colon tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-121, 123-197 and 205-486.

COLON TUMOR PROTEIN POLYNUCLEOTIDES

5

10

15

20

25

30

Any polynucleotide that encodes a colon tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a colon tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a colon tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a colon tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native colon tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and

10

15

20

25

30

compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy* – the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of

hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native colon tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a colon tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as colon tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a colon tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide

5

10

15

20

probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ³²P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by

5

10

15

20

25

amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic. 1*:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids Res. 19*:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding portions of colon tumor proteins are provided in SEQ ID NO: 1-121, 123-197 and 205-486. These polynucleotides were isolated from colon tumor cDNA libraries using conventional and/or PCR-based subtraction techniques, as described below.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding a colon tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo (e.g., by transfecting

5

10

15

20

25

10

15

20

25



antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a colon tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In

general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

COLON TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a colon tumor protein or a variant thereof, as described herein. As noted above, a "colon tumor protein" is a protein that is expressed by colon tumor cells. Proteins that are colon tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with colon cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or

5

10

15

heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a colon tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native colon tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, 125I-labeled Protein A.

As noted above, a composition may comprise a variant of a native colon tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native colon tumor protein in one or more substitutions, deletions, additions and/or insertions, such

5

10

15

20

25

WO 00/37643 36 PCT/US99/30909

that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain non-conservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

5

10

15

20

25

5

10

15

20

25

30

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide:

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A

fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

PCT/US99/30909

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene 40*:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA 83*:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and

5

10

15

20

25

second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene 43*:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid

5

10

15

20

25

WO 00/37643 40 PCT/US99/30909

proteins containing the C-LYTA fragment at the amino terminus has been described (see Biotechnology 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

5

10

15

20

25

30

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a colon tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a colon tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a colon tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10³ L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as colon cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a colon tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies

this requirement, biological samples (e.g., blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example,

5

10

15

20

25

WO 00/37643 42 PCT/US99/30909

from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid.

5

10

15

20

25

5

10

15

20

25

30

Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

WO 00/37643 44 PCT/US99/30909

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

25

30

20

5

10

15

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a colon tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEXTM system, available from

WO 00/37643 45 PCT/US99/30909

Nexell Therapeutics Inc., Irvine, CA. Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a colon tumor polypeptide, polynucleotide encoding a colon tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a colon tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a colon tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the T cell specificity may be evaluated using any of a variety of standard polypeptide. For example, within a chromium release assay or proliferation assay, a techniques. stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a colon tumor polypeptide (100 ng/ml - 100 μg/ml, preferably 200 ng/ml - 25 μg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a colon tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4+ and/or CD8+. Colon tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a colon tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro*

5

10

15

20

25

WO 00/37643 46 PCT/US99/30909

or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a colon tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a colon tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a colon tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the

5

10

15

20

25

necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., Proc. Natl. Acad. Sci. USA 86:317-321, 1989; Flexner et al., Ann. N.Y. Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0.345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., Proc. Natl. Acad. Sci. USA 91:215-219, 1994; Kass-Eisler et al., Proc. Natl. Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and

5

10

15

20

25

WO 00/37643 48 PCT/US99/30909

5,075,109.

5

10

15

20

25

30

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, TNFα, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, Ann. Rev. Immunol. 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical

5

10

15

20

25

WO 00/37643 50 PCT/US99/30909

compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see Zitvogel et al.*, *Nature Med. 4*:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

5

10

15

20

25

WO 00/37643 PCT/US99/30909

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a colon tumor protein (or portion or other variant thereof) such that the colon tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the colon tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a nonconjugated immunological partner, separately or in the presence of the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as colon cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or

5

10

15

20

25

WO 00/37643 52 PCT/US99/30909

may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8* cytotoxic T lymphocytes and CD4* T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive

30

5

15

20

polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews 157*:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to nonvaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient,

5

10

15

20

25

WO 00/37643 54 PCT/US99/30909

but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a colon tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more colon tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as colon cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a colon tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of

5

10

15

20

25

the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length colon tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

30

5

10

15

20

WO 00/37643 PCT/US99/30909

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with colon cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

5

10

15

20

25

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as colon cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

5

10

15

20

25

WO 00/37643 58 PCT/US99/30909

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use colon tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such colon tumor protein specific antibodies may correlate with the presence of a cancer.

5

10

15

20

25

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a colon tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a colon tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with one or more representative polypeptides (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of colon tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a colon tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a colon tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the colon tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a colon tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a colon tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will

5

10

15

20

25

WO 00/37643 60 PCT/US99/30909

hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-121, 123-197 and 205-486. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may

5

10

15

20

25

WO 00/37643 PCT/US99/30909

also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple colon tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

10

15

20

25

5

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a colon tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a colon tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a colon tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a colon tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

WO 00/37643 PCT/US99/30909

EXAMPLES

5

10

15

20

25

30

Example 1

ISOLATION AND CHARACTERIZATION OF COLON TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION AND MICROARRAY ANALYSIS

A cDNA library was constructed in the PCR2.1 vector (Invitrogen, Carlsbad, CA) by subtracting a pool of three colon tumors with a pool of normal colon, spleen, brain, liver, kidney, lung, stomach and small intestine using PCR subtraction methodologies (Clontech, Palo Alto, CA). The subtraction was performed using a PCR-based protocol, which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (Mlul, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with Rsal according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs, and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not

hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are over-expressed in colon tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

To characterize the complexity and redundancy of the subtracted library, 96 clones were randomly picked and 65 were sequenced, as previously described. These sequences were further characterized by comparison with the most recent Genbank database (April, 1998) to determine their degree of novelty. No significant homologies were found to 21 of these clones, hereinafter referred to as 11092, 11093, 11096, 11098, 11103, 11174, 11108, 11112, 11115, 11117, 11118, 11134, 11151, 11154, 11158, 11168, 11172, 11175, 11184, 11185 and 11187. The determined cDNA sequences for these clones are provided in SEQ ID NO: 48, 49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101 and 109-111, respectively.

Two-thousand clones from the above mentioned cDNA subtraction library were randomly picked and submitted to a round of PCR amplification. Briefly, 0.5 µl of glycerol stock solution was added to 99.5 µl of pcr MIX (80 µl H₂0, 10 µl 10X PCR Buffer, 6 μl 25 mM MgCl₂, 1 μl 10 mM dNTPs, 1 μl 100 mM M13 forward primer M13 (CACGACGTTGTAAAACGACGG), 1 μl 100 mM reverse primer (CACAGGAAACAGCTATGACC)), and 0.5 µl 5 u/ml Taq polymerase (primers provided by (Operon Technologies, Alameda, CA). The PCR amplification was run for thirty cycles under the following conditions: 95°C for 5 min., 92°C for 30 sec., 57°C for 40 sec., 75°C for 2 min. and 75°C for 5 minutes.

mRNA expression levels for representative clones were determined using microarray technology (Synteni, Palo Alto, CA) in colon tumor tissues (n=25), normal colon tissues (n=6), kidney, lung, liver, brain, heart, esophagus, small intestine, stomach, pancreas, adrenal gland, salivary gland, resting PBMC, activated PBMC, bone marrow, dendritic cells, spinal cord, blood vessels, skeletal muscle, skin, breast and fetal tissues. The number of tissue samples tested in each case was one (n=1), except where specifically noted above; additionally, all the above-mentioned tissues were derived from humans. The PCR

5

10

15

20

25

WO 00/37643 64 PCT/US99/30909

amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, and fluorescent-labeled cDNA probes were generated by reverse transcription according to the protocol provided by Synteni. The microarrays were probed with the labeled cDNA probes, the slides scanned, and fluorescence intensity was measured. This intensity correlates with the hybridization intensity.

One hundred and forty nine clones showed two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group. These cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). These sequences were compared to known sequences in the most recent GenBank database. No significant homologies to human gene sequences were found in forty nine of these clones, represented by the following sixteen cDNA consensus sequences: SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46 and 47, hereinafter referred to as Contig 2, 8, 13, 14, 20, 23, 29, 31, 35, 32, 36, 38, 41, 42, 50 and 51, respectively). Contig 29 (SEQ ID NO: 30) was found to be a Rat GSK-3-β-interacting protein Axil homolog. Also, Contigs 31 and 35 (SEQ ID NO: 32 and 33, respectively) were found to be a Mus musculus GOB-4 homolog. The determined cDNA sequences of SEQ ID NO: 1, 3-7, 9-14, 17-21, 23, 25-29, 31, 35, 37, 39, 42-45, 50, 51, 53, 55-58, 61-64, 70-78, 80-88, 91, 92, 94-98, 102-108 and 112 were found to show some homology to previously identified genes sequences.

Microarray analysis demonstrated Contig 2 (SEQ ID NO: 2) showed over-expression in 34% of colon tumors tested, as well as increased expression in normal pancreatic tissue, with no over-expression in normal colon tissues. Upon further analysis, Contigs 2, 8 and 23 were found to share homology to the known gene GW112. Contigs 4, 5, 9 and 52 showed homology to carcinoembryonic antigen (SEQ ID NO: 3, 4, 5 and 6, respectively). A representative sampling of these fragments showed over-expression in 85% of colon tumors, with over-expression in normal bone marrow and 3/6 normal colon tissues. Contig 6 (SEQ ID NO: 7), showing homology to the known gene sequence for villin, and was over-expressed in about half of all colon tumors tested, with a limited degree of Tow level over-expression in normal colon. Contig 12 (SEQ ID NO: 14), showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P, was over-expressed in

5

10

15

20

25

approximately 70% of colon tumors tested, with low over-expression in 1/6 normal colon samples. Contig 14, also referred to as 14261 (SEQ ID NO: 16), showing no significant homology to any known gene, showed over-expression in 44% of colon tumors tested, with low level expression in half of normal colon tissues, as well as small intestine and pancreatic tissue. Contig 18 (SEQ ID NO: 21), showing homology to the known gene for L1-cadherin, showed over-expression in approximately half of colon tumors and low level over-expression in 3/6 normal colon tissues tested. Contig 22 (SEQ ID NO: 23), showing homology to Bumetanide-sensitive Na-K-Cl cotransporter was over-expressed in 70% of colon tumors and no over-expression in all normal tissues tested. Contig 25 (SEQ ID NO: 25), showing homology to macrophage inflammatory protein-3a, was over-expressed in over 40% of colon tumors and in activated PBMC. Contigs 26 and 48 (SEQ ID NOS: 25 and 26), showing homology to the sequence for laminin, was over-expressed in 48% of colon tumors and with low over-expression in stomach tissue. Contig 28 (SEQ ID NO: 29), showing homology to the known gene sequence for Chromosome 16 BAC clone CIT987SK-A-363E6; was overexpressed in 33% of colon tumors tested with normal stomach and 2/6 normal colon tissues showing low level over-expression. Contigs 29, 31 and 35 (SEQ ID NOS: 30, 32 and 33, respetively), also referred to as C751P, an unknown sequence showing limited and partial homology to Rat GSK-3\beta-interacting protein Axil homolog.and Mus musculus GOB-4 homolog, was over-expressed in 74% of colon tumors and no over-expression in all normal tissues tested. Contig 34 (SEQ ID NO: 35), showing homology to the known sequence for desmoglein 2, was over-expressed in 56% of colon tumors and showed low level overexpression in 1/6 normal colon tissues. Contig 36 (SEQ ID NO: 36), an unknown sequence also referred to as C793P, showed over-expression in 30% of colon tumor tissues tested. Contig 37 and 14287.2 (SEQ ID NOS: 37 and 116), an unknown sequence, but with limited (89%) homology to the known sequence for putative transmembrane protein was overexpressed in 70% of colon tumors, as well as in normal lung tissue and 3/6 normal colon tissues tested. Contig 38, also referred to as C796P and 14219 (SEQ ID NO: 38), showing no significant homology to any known gene, was over-expressed in 38% in colon tumors and no elevated over-expression in any normal tissues. Contig 41 (SEQ ID NO: 40), also referred to as C799P and 14308, an unknown sequence showing no significant homology to any known gene, was over-expressed in 22% of colon tumors. Contig 42, (SEQ ID NO: 41), also

5

10

15

20

25

WO 00/37643 PCT/US99/30909

referred to as C794P and 14309, an unknown sequence with no significant homology to any known gene, was over-expressed in 63% of colon tumors tested, as well as in 3/6 normal colon tissues. Contig 43 (SEQ ID NO: 42), showing homology to the known sequence for Chromosome 1 specific transcript KIAA0487 was over-expressed in 85% of colon tumors tested and in normal lung and 4/6 normal colon tissues. Contig 49 (SEQ ID NO: 45), showing homology to the known sequence for pump-1, was over-expressed in 44% of colon tumors and no over-expression in all normal tissues tested. Contig 50 (SEQ ID NO: 46), also referred to as C792P and 18323, showing no significant homology to any known gene, was over-expressed in 33% of colon tumors with no detectable over-expression in any normal tissues tested. Contig 51 (SEQ ID NO: 47), also referred to as C795P and 14317 was over-expressed in 11% of colon tumors.

Additional microarray analysis yielded seven clones showing two or more fold overexpression in the colon tumor probe group as compared to the normal tissue probe group. Three of these clones demonstrated particularly good colon tumor specificity, and are represented by SEQ ID NO: 115, 116 and 120. Specifically, SEQ ID NO: 115, referred to as C791P or 14235, which shows homology to the known gene sequence for H. sapiens chromosome 21 derived BAC containing ets-2 gene, was over-expressed in 89% of colon tumors tested and in 5/6 normal colon tissues, as well as over-expressed at low levels in normal lung and activated PBMC. Microarray analysis for SEQ ID NO: 116 is discussed above. SEQ ID NO: 120, referred to as 14295, showing homology to the known gene sequence for secreted cement gland protein XAG-2 homolog, was over-expressed in 70% of colon tumors and in 5/6 normal colon tissues, as well as low level over-expression in normal small intestine, stomach and lung. All clones showing over-expression in colon tumor were sequenced and these sequences compared to the most recent Genbank database (February 12, Of the seven clones, three contained sequences that did not share significant homology to any known gene sequences, represented by SEQ ID NO: 116, 117 and 119. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in colon. The determined cDNA sequences of the remaining clones (SEQ ID NO: 113-115 and 120) were found to show some homology to previously identified genes.

Further analysis identified a clone which was recovered several times by PCR subtraction and by expression screening using a mouse anti-scid antiserum. The determined

5

10

15

20

25

full length cDNA sequence for this clone is provided in SEQ ID NO: 121, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 122. This clone is homologous with the known gene Beta IG-H3, as disclosed in U.S. Patent No. 5,444,164. Microarray analysis demonstrated this clone to be over-expressed in 75 to 80% of colon tumors tested (n=27), with no over-expression in normal colon samples (n=6), but with some low level over-expression in other normal tissues tested.

Further analysis of the PCR-subtraction library described above led to the isolation of longer cDNA sequences for the clones of SEQ ID NO: 30, 115, 46, 118, 41, 47, 38, 113, 14 and 40 (known as C751P, C791P, C792P, C793P, C794P, C795P, C796P, C797P, C798P and C799P, respectively). These determined cDNA sequences are provided in SEQ ID NO: 123-132, respectively.

Using PCR subtraction methodology described above with minor modifications, transcripts from a pool of three moderately differentiated colon adenocarcinoma samples were subtracted with a set of transcripts from normal brain, pancreas, bone marrow, liver, heart, lung, stomach and small intestine. Modifications of the above protocol were included at the cDNA digestion steps and in the tester to drive hybridization ratios. In a first subtraction, the restriction enzymes PvuII, DraI, MscI and StuI were used to digest cDNAs, and the tester to driver ratio was 1:40, as suggested by Clontech. In a second subtraction, DraI, MscI and StuI were used for cDNA digestion and a tester to driver ratio of 1:76 was used. Following the PCR amplification steps, the cDNAs were clones into pCR2.1 plasmid vector. The determined cDNA sequences of 167 isolated clones are provided in SEQ ID NO: 205-371. These sequences were compared to sequences in the public databases as described above. The sequences of SEQ ID NO: 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369 and 371 were found to show some homology to previously identified ESTs. The remaining sequences were found to show some homology to previously identified genes.

Using the PCR subtraction technology described above, a cDNA library from a pool of primary colon tumors was subtracted with a cDNA library prepared from normal tissues, including brain, bone marrow, kidney, heart, lung, liver, pancreas, small intestine,

5

10

15

20

25

WO 00/37643 68 PCT/US99/30909

stomach and trachea. The determined cDNA sequences for 90 clones isolated in this subtraction are provided in SEQ ID NO: 372-461. Comparison of these sequences with those in the public databases as described above, revealed no homologies to the sequences of SEQ ID NO: 426, 445 and 453. The sequences of SEQ ID NO: 372-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455 and 457-461 showed some homology to previously identified genes, while the sequences of SEQ ID NO: 379, 405, 407, 408, 418, 424, 430-432, 437, 442, 444, 452 and 456 showed some homology to previously isolated ESTs.

10

15

20

25

30

5

Example 2

<u>ISOLATION OF TUMOR POLYPEPTIDES</u> <u>USING SCID-PASSAGED TUMOR RNA</u>

Human colon tumor antigens were obtained using SCID mouse passaged colon tumor RNA as follows. Human colon tumor was implanted in SCID mice and harvested, as described in Patent Application Serial No. 08/556,659 filed 11/13/95, U.S. Patent No. 5,986,170. First strand cDNA was synthesized from poly A+ RNA from three SCID mouse-passaged colon tumors using a Lambda ZAP Express cDNA synthesis kit (Stratagene). The reactions were pooled and digested with RNase A, T1 and H to cleave the RNA and then treated with NaOH to degrade the RNA. The resulting cDNA was annealed with biotinylated (Vector Labs, Inc., Burlingame, CA) cDNA from a normal resting PBMC plasmid library (constructed from Superscript plasmid System, Gibco BRL), and subtracted with streptavidin by phenol/chloroform extraction. Second strand cDNA was synthesized from the subtracted first strand cDNA and digested with S1 nuclease (Gibco BRL). The cDNA was blunted with Pfu polymerase and EcoRI adaptors (Stratagene) were ligated to the ends. The cDNA was phosphorylated with T4 polynucleotide kinase, digested with restriction endonuclease XhoI, and size selected with Sephacryl S-400 (Sigma). Fractions were pooled, ligated to Lambda ZAP Express arms (Stratagene) and packaged with Gigapack Gold III extract (Stratagene). Random plaques were picked, phagemid was excised, transformed into XLOLR cells (Stratagene) and resulting plasmid DNA (Qiagen Inc., Valencia, CA) was sequenced as described above. The determined cDNA sequences for 17

clones isolated as described above are provided in SEQ ID NO: 133-151, wherein 133 and 134 represent partial sequences of a clone referred to as CoSub-3 and SEQ ID NO: 135 and 136 represent partial sequences of a clone referred to as CoSub-13. These sequences were compared with those in the public databases as described above. The sequences of SEQ ID NO: 139 and 149 showed no significant homologies to any previously identified sequences. The sequences of SEQ ID NO: 138, 140, 141, 142, 143, 148 and 149 showed some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 133-137, 144-147, 150 and 151 showed some homology to previously isolated gene sequences.

10

15

20

25

30

5

Example 3

USE OF MOUSE ANTISERA TO IDENTIFY DNA SEQUENCES ENCODING COLON TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding colon tumor antigens by screening of colon tumor cDNA libraries with mouse anti-tumor sera.

A cDNA expression library was prepared from SCID mouse-passaged human colon tumor poly A+ RNA using a Stratagene (La Jolla, CA) Lambda ZAP Express kit, following the manufacturer's instructions. Sera was obtained from the colon tumor-bearing SCID mouse. This serum was injected into normal mice to produce anti-colon tumor serum. Approximately 600,000 PFUs were screened from the unamplified library using this antiserum. Using a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (BRL Labs.), positive plaques were identified. Phage was purified and phagemid excised for several clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined cDNA sequences for 46 of the isolated clones are provided in SEQ ID NO: 152-197. The predicted amino acid sequences for the cDNA sequences of SEQ ID NO: 187, 188, 189, 190, 194, 195 and 197 are provided in SEQ ID NO: 198-204, respectively. The determined cDNA sequences were compared with those in the public database as described above. The sequences of SEQ ID NO: 156, 168, 184, 189, 192 and 196 showed some homology to previously isolated ESTs. The sequences of SEQ ID NO: 152-

WO 00/37643 70 PCT/US99/30909

155, 157-167, 169-182, 183, 185-188, 190, 194, 195 and 197 showed some homology to previously identified genes.

Example 4

ISOLATION AND CHARACTERIZATION OF COLON TUMOR POLYPEPTIDES BY CONVENTIONAL SUBTRACTION

Two cDNA libraries were constructed and used to create a subtracted cDNA library as follows.

Using the GibcoBRL Superscript Plasmid System with minor modifications, two cDNA libraries were created. The first library, referred to as CTCL, was prepared from a pool of mRNA samples from three colon adenocarcinoma tissue samples. Two of the samples were described as Duke's stage C and one as Duke's stage B. All three samples were grade III in histological status. A second library (referred to as DriverLibpcDNA3.1+) was prepared from a pool of normal tissues, namely liver, pancreas, skin, bone marrow, resting PBMC, stomach and brain. Both libraries were prepared using the manufacturer's instructions with the following modifications: an EcoRI-NotI 5' cDNA adapter was used instead of the provided reagent; the vector pCDNA3.1(+) (Invitrogen) was substituted for the pSPORT vector; and the ligated DNA molecules were transformed into ElectroMaxDH10B electrocompetent cells. Clones from the libraries were analyzed by restriction digest and sequencing to determine average insert size, quality of the library and complexity of the library. DNA was prepared from each library and digested.

The driver DNA was biotinylated and hybridized with the colon library tester DNA at a ratio of 10:1. After two rounds of hybridizations, streptavidin incubations and extractions, the remaining colon cDNAs were size-selected by column chromatography and cloned into the pCMV-Script vector from Stratagene. Clones from this subtracted library (referred to as CTCL-S1) were characterized as described above for the unsubtracted libraries.

The determined cDNA sequences for 18 clones isolated from the CTCL-S1 library are provided in SEQ ID NO: 462-479. Comparison of these sequences with those in the public databases, as described above, revealed no significant homologies to the sequences

5

10

15

20

25

WO 00/37643 71 PCT/US99/30909

of SEQ ID NO: 476, 477 and 479. The remaining sequences showed some homology to previously identified genes.

In further studies, a cDNA library was prepared from a pool of mRNA from three metastatic colon adenocarcinomas derived from liver tissue samples. All samples were described as Duke's stage D. Conventional subtraction was performed as described above, using the DriverLibpcDNA3.1+ library described above as the driver. The resulting subtracted library (referred to as CMCL-S1) was characterized by isolating a set of clones for restriction analysis and sequencing.

The determined cDNA sequences for 7 clones isolated from the CMCL-S1 library are provided in SEQ ID NO: 480-486. Comparison of these sequences with those in the public databases revealed no significant homologies to the sequence of SEQ ID NO: 483. The sequences of SEQ ID NO: 480-482 and 484-486 were found to show some homology to previously identified genes.

Example 5 SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

10

15

20

25

WO 00/37643



PCT/US99/30909

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

10

15

20

25

CLAIMS

- 1. An isolated polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
 - (a) sequences recited in SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483;
 - (b) sequences that hybridize to a sequence of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 under moderately stringent conditions; and
 - (c) a complement of a sequence of (a) or (b).
- 2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168,

WO 00/37643

170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing polynucleotide sequences.

PCT/US99/30909

- 3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 122 and 198-204.
- An isolated polynucleotide encoding at least 15 amino acid residues of 10 4. a colon tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 15 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 20 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing sequences.
- 5. An isolated polynucleotide encoding a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303,



310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing sequences.

- 6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483.
- 7. An isolated polynucleotide comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-15 49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 20 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 under moderately stringent conditions.
- 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7. 25
 - 9. An expression vector comprising a polynucleotide according to any one of claims claim 4-8.
- 30 10. A host cell transformed or transfected with an expression vector according to claim 9.

5



- 11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a colon tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing polynucleotide sequences.
- 12. A fusion protein comprising at least one polypeptide according to claim 1.
 - 13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

5

- 14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.
 - 16. An isolated polynucleotide encoding a fusion protein according to claim 12.
- 17. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.
- 18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:
 - (a) a polypeptide according to claim 1;
 - (b) a polynucleotide according to claim 4;
 - (c) an antibody according to claim 11;
 - (d) a fusion protein according to claim 12; and
 - (e) a polynucleotide according to claim 16.
- 19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.
- 20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.
- 21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.
- 25. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.
- A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically
 acceptable carrier or excipient.

10

15

24.

antigen presenting cell is a dendritic cell or a macrophage.

- A pharmaceutical composition according to claim 23, wherein the
- 25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.
 - 26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.
- 27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.
 - 28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486, and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

- 31. A method according to any one of claims 21, 22 and 29, wherein the cancer is colon cancer.
 - 32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
 - (i) polynucleotides recited in any one of SEQ ID NO: 1-121, 123-

15

20

25

197 and 205-486; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

5

- 33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.
- 34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.
- 35. A method for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:
 - (i) a polypeptide according to claim 1;
 - (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-121, 123-197 and 205-486;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
 - (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

- 36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.
- 37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

30

20

25

38. A method for inhibiting the development of a cancer in a patient,

comprising the steps of:

- (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
 - (i) a polypeptide according to claim 1;

5

- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-121, 123-197 and 205-486;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or

10 (ii);

such that T cells proliferate; and

- (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.
- 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
 - (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
 - (i) a polypeptide according to claim 1;

20

15

- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-121, 123-197 and 205-486;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iii) an antigen-presenting cell that expresses a polypeptide of (i) or

25 (ii);

such that T cells proliferate;

- (b) cloning at least one proliferated cell to provide cloned T cells; and
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

30

40. A method for determining the presence or absence of a cancer in a

WO 00/37643 PCT/US99/30909

patient, comprising the steps of:

5

10

15

20

25

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (i) polynucleotides recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486; and
 - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 41. A method according to claim 40, wherein the binding agent is an antibody.
- 42. A method according to claim 43, wherein the antibody is a monoclonal antibody.
 - 43. A method according to claim 40, wherein the cancer is colon cancer.
- 44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- 30 (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 45. A method according to claim 44, wherein the binding agent is an antibody.
 - 46. A method according to claim 45, wherein the antibody is a monoclonal antibody.
- 10 47. A method according to claim 44, wherein the cancer is a colon cancer.
 - 48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
 - (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;
 - (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
 - (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
 - 50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
 - 51. A method for monitoring the progression of a cancer in a patient,

15

WO 00/37643 PCT/US99/30909

comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
 - 53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

20

5

10

15

- 54. A diagnostic kit, comprising:
- (a) one or more antibodies according to claim 11; and
- (b) a detection reagent comprising a reporter group.
- 55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.
 - 56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
- 30

25

57. A kit according to claim 54, wherein the reporter group is selected

from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

- 58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing polynucleotides.
 - 59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483.

25

15

- 60. A diagnostic kit, comprising:
- (a) an oligonucleotide according to claim 59; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

SEQUENCE LISTING

<110> Corixa Corporation <120> COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE <130> 210121.471PC <140> PCT <141> 1999-12-23 <160> 486 <170> FastSEQ for Windows Version 3.0 <210> 1 <211> 458 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(458) <223> n = A, T, C or G<400> 1 ncaggtctgg cggcacctgt gcactcagcc gtcgatacac tggtcgattg ggacagggaa 60 gacgatgtgs ttttcaggga ggcccagaga tttggagaag cggatgaagt tctcctttag 120 ttccgaagtc agotocttgg ttctcccgta gagggtgatc ttgaagtact ccctgttttg 180 agaaactttc ttgaagaaca ccatagcatg ctggttgtag ttggtgctca ccactcggac 240 gaggtaactc gttaatccag ggtaactctt aatgttgccc agcgtgaact cgccgggctg 300 gcaacctgga acaaaagtcc tgatccagta gtcacacttc tttttcctaa acaqqacqqa 3.60 ggtgacattg tagetettgt cttettteag eteatagatg gtggeataea tettttgegg 420 gtctttgtct tctctgagaa ttgcattccc tgccagga 458 <210> 2 <211> 423 <212> DNA <213> Homo sapien <400> 2 cagggtccat aggtgatccg caactctcga gcatttatat acaatagcaa atcatccagt 60 gtgttgtaca gtctataata ctccaacagt ctcccatctg tattcaatgg cgccacccaa 120 tacagteett tgtttggatg etggggagag taateeetae eccaageace atatagataa 180 gaaaaccctc tccagttgag ctgaaccaca gacggtttgc tgatgttcac cacaccacca 240 tgaccacage teeetggagt gggaggaggg.xtggacgacag gggtgttttg atetttagag 300 - 37% gcttcacact ctttcagctt ggtcttcaga gccacgattt ctcggcgaat ggcaaggaca 360 ttgtttttgt ctagtgtctc aagettetet accaagagag teatatttet tatetecace 420 423

tcc

<210> 3 <211> 538

```
<212> DNA
        <213> Homo sapien
       <400> 3
 ggtctgtcca atggcaacag gaccetcact ctaytcartg tcacaagraa tgayrcagsa
                                                                         60
 msctayraat gtgaaaycca gaacccagtg agtgccarsc gcagtgayyc agtcatcctg
                                                                         120
 aatgteetet atggeeerga tgmeeecace attteeeete taaacacatm ttaeegwyca
                                                                         180
 ggggaaaatc tgaacctctc ctgccacgca gcctctaacc cacctgcaca gtactcttgg
                                                                        240
 tttrtcaatg ggactttcca gcaatccacm caagagctct ttatccccaa catcactgtg
                                                                        300
 aataatagyg gateetatae gtgeeaagee cataacteag meaetggeet caataggaee
                                                                        360
 acagtcacga cgatcacagt ctatgcaaga gccacccaaa cccttcatca ccagcaacaa
                                                                        420
 ctccaacccc gtggaggatg aggatgctgt agccttaacc tgtgaacctg agattcagaa
                                                                        480
 cacaacctac ctgtggtggg taaataatca gagcctcccg gtcagtccca ggctgcag
                                                                        538
       \leq 2.1.0 \geq 4
       <211> 309
       <212> DNA
       <213> Homo sapien
       <400> 4
tggtaascca aaaagatgct ggggcagatt gtggacaagt agaagaacct ccttccctc
                                                                        . 60
tgcgaacatt gaacggcgtg gattcaatag tgagcttggc agtggtgggc gggttccaga
aggttagaag tgaggetgtg agcaggagee cetgecaggg gatveacgea mtetgtgggg
                                                                        120
                                                                        180
aggggctgag rggdgwcycc atggtctctg ctgtctgctc tgtcctcctc tgtggagaag
                                                                        240
agettgaget ccaggaacge tttgrtcavg getgeetgtg acetytgete tgbtetgeet
                                                                        300
gcccgggcg
                                                                        309
       <210> 5
       <211> 412
       <212> DNA
       <213> Homo sapien ...
gtccaatggc aacaggaccc ctcacttcta ttcaatgtca caagaaatga cgcaagagcc
                                                                        60
tatgtatgtg gaatccagaa ctkcagtgag tgcaaaccgc agtgacccag tcaccctgga
                                                                       120
tgtcctctat gggccagaca scccccatca tttccccccc agactcgtct tacctttcgg
                                                                       180
gagegaacet caacetetee tgccactegg cetetaacee ateccegeag tattettgge
                                                                       240
kgtatcaatg ggataccgca gcaacacaca caagttctct ttatcgccaa aatcacgcca
                                                                       300
aataataacg ggacctatgc ctgttttgtc tctaacttgg ctactggccc gcaataattc
                                                                       360
catagtcaag agcatcacag tettetgcat etggaactte teetggtett et
                                                                       412
      <210> 6
      <211> 332
      <212> DNA
      <213> Homo sapien
      <400> 6
gtgcaagggc tttacaaaaa ctgtgccagt krcttctyca tgwsrcwrga tctgacttka
ttsaygttkt atgagsysya saatmetgaw getemttyts sakgrwstterkgsatmrgea
                                                                        60
gtsrattcsa catttgggrt akrtymtctc tsgaagysam tgtcakgcag tgrcayccwr
                                                                       120
                                                                       180
gkktcwgcwt gcwgtgrgtt amcakcmwtr ywtagkgsgm ayatrattta ramrgtayak
cymtctcmct cytycmccay wtgcwcaass mkcacacctc ggccgcgacc acgctaagcc
                                                                       240
                                                                       300
cgaattccag cacactggcg gccgttacta gt
                                                                       332
```

<210> 7

```
<211> 401
      <212> DNA
      <213> Homo sapien
      <400> 7
tggtgttgtt ggcgccagtt ccctggacct ggaacagccg tgtggagggc ccggtctcca
                                                                         60
agttgttagt tegggaggtg cetecetggt agaccaccat gegteeettg aagatggaca
                                                                        120
taagatgagg tggctccttg cccattggga cccggatctg gactggttca ccattgtact
                                                                        180
totggtocag gatgacggot tgataagotg atgotgtaat ttoatottgg ctggcotggo
                                                                        240
tgccctgcca aacgtagagc aggtaatgct gcttctcgcc gatgaaggta ggtgtaagag
                                                                        300
cagcaggtaa gcaagttege ceccatagaa gtgggeetag cesettggaa ttecagcaca
                                                                        360
ctggcggccc gttactagtg.ggatcccgag ctcggtacca a
                                                                        401
      <210> 8
      <21.1> 1151
      <212> DNA
      <213> Homo sapien
      <400> 8
ctctctccat aaaactcage actttacaga tgtagaatat ataagcatge caaatttact.
                                                                        60
tatotgocac atacaaagca toattocagg tgotagtgag gggaaaaaaa agttggagat
                                                                        120
ttggtccctc gaggagetec agatattaat ctacetaaet aagteeceag gtttetteca
                                                                        180
ggcatggaag aattagtggt gctacatgga tgaggactag tcattgggca atatttcctg
                                                                       240
tacaaagaat ccctagacgc catactgagt tttaagttcc ttaattccta atttaaggct
                                                                        300
totagtgaag cotoctcaca gtaggottca ctaggoccac agtgedecta gacotetgae
                                                                        360
aatoccacco tagacagact ttattgcaaa atgcgcctga agaggcagat gattcccaag
                                                                        420
agaactcacc aaatcaagac aaatgtccta gatctctagt gtggtagaac tatgcaccta
                                                                        480
aacattgctg caaaatgaac acacttttag acacccctgc agatatctaa gtaagtggag
                                                                        540
aagactattt tttcaacaaa cattttctct ttcaccctaa ctcctaaaca gcttactggg
                                                                        600
gcttctgcaa gacagaaaga tcataattca gaaggtaacc atcgttatag acataaagtt
                                                                        660
tctggtcaaa agggttatag ttaatgctct gcactttttc ctgcatctta tgcattacaa
                                                                        720
tgtctagttt gccctctttc cctgtgtttg tgtcataata gtaaaaaatc tcttctgttc
                                                                        780
tggtgtttca tagtacgggt ggcatacaga accccacata ccatgaaggc gttagaagca
                                                                      840
gatggtttat actgcttggt ataccaagtg tttagcacct gaagtgtggt gtcattgagt
                                                                        900
ttactaatca ccatgttacc agtgctggct tcagttgaat aaataaccca caatccattc
                                                                       960
tcatccacag caaagtcaat atcttgccaa gcaacattag catatgaaaa gcggttatta
                                                                       1020
taggcagcat tagggagagt ttgagtcaca gcaatcgtgt tggtggtcag gttaactctg
                                                                       1080
gcaatattcc cggtgttgta catgttgacg tacatgttgt tgttgtaaac tgctgtacca
                                                                       1140
ctaccttgga c
                                                                       1151
      <210> 9
      <211> 604
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(604)
      <223> n = A, T, C \text{ or } G
ctgtgcaagg gctttacaaa aactgtgcca ggacttccca tgaggctgga ttgcttgatt
                                                                        60
catgttttat gagccccaca atactgaagc teetttteca gggaettgge ataggcagte
                                                                       120
aattccacat ttgggatagg tcctctctgg aagtgaatgt caggcagtga catccaagtt
                                                                       180
tctgcatgca gtgggttaac agccatgttt agggggaaca tgatttaaaa agtacatctc
                                                                       240
```

tctccctct ccccacatg cacaagga attaaagtgt gatacttkgg ttttgaaa gaaattggcg gagagetgcc gtggtgca tcctttntta ataacttttg atagacag gaaaacgctg atgcttgttt gaagateg tcctgaggtc tgttggctgg aggctgcagtgg	aac attcaaacag att cctcctgtag ggg gctagtcgca cca agcgcagagt	tctctgtgga tgcttcaagn cagacctctg ctgcaagttc	aatctggaga taatgcttca ggaagccctg atcccctctt	300 360 420 480 540 600
<210> 10				
<211> 473				
<212> DNA	•••			
<213> Homo sapien				
<400> 10				
tcgagaagat ccctagtgag actttgaa				60
acctgctgaa caaccacatc ttgaagto				120
tgtctgtgga gaccctggag ggcacgad				180
ctatcaacgg gaaggcgatc atctccaa				240
actacattga tgagctactc atcccaga				30.0
agtotgatgt gtocacagco attgacot				360
ctggaagtga gcggttgacc ctcctggg				420
cctccaattg atgcccatac aaggaatt	.cg ccccggaacc	acacaaccaa	aya .	473
<210> 11				
<211> 411				
<212> DNA	•			
<213> Homo sapien				
<220>				
	•			
<221> misc_feature	•			
<221> misc_feature <222> (1)(411)				
<221> misc_feature				
<221> misc_feature <222> (1)(411) <223> n = A,T,C or G	•			
<221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11	ac togggattac	crtcaagcat	. Catattaaaa	60
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgt</pre>				60
<221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaaggg	gtc tcaaaggtgt	cctcgatctc	aatgatctgc	120
<221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgt cctgatgcag ccacagcagc ccgaaggg tggatgttgt tggtgatggt ggagatga	gtc tcaaaggtgt acc ttatcgatga	cctcgatctc ggtgcaccac	aatgatctgc cccgttggtt	120 180
<221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgaggcatggtgt cggctttyar carccggg	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag	cctcgatctc ggtgcaccac ttacaatccc	aatgatctgc cccgttggtt attaggatag	120 180 240
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatgt ggagatgt ggatgttgt cggctttyar carccgggtggtggtggatct nggatgttgg aattctgg</pre>	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat	aatgatctgc cccgttggtt attaggatag gcccgtgttt	120 180
<221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgaggcatggtgt cggctttyar carccggg	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag	120 180 240 300
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgt cctgatgcag ccacagcagc ccgaaggg tggatgttgt tggtgatggt ggagatgg tggtggt cggctttyar carccggg tggtggatct nggatgttgg aattctgg cagctcatca gtcaggactc gcctgccg</pre>	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag	120 180 240 300 360
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgatgcatggtggt cggctttyar carccgggtggtggtggtcatca gtcaggactc gcctgcccctcaatgtt gacattgctg gaccaggg</pre> <210> 12	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag	120 180 240 300 360
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgatggtggtggtcttyar carcegggtggtggtggtcatca gtcaggactc gcctgcccctcaatgtt gacattgctg gaccaggg</pre> <210> 12 <211> 560	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag	120 180 240 300 360
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgggcatggtggt cggctttyar carccgggtggtggtggatct nggatgttgg aattctggcagctcatca gtcaggactc gcctgccctcaatgttt gacattgctg gaccaggg</pre> <210> 12 <211> 560 <212> DNA	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag	120 180 240 300 360
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgatggtggtggtcttyar carcegggtggtggtggtcatca gtcaggactc gcctgcccctcaatgtt gacattgctg gaccaggg</pre> <210> 12 <211> 560	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag	120 180 240 300 360
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgggcatggtggt cggcttyar carccgggtggtggatct nggatgttgg aattctggcagctcatca gtcaggactc gcctgccctcaatgtt gacattgctg gaccaggg <210> 12 <211> 560 <212> DNA <213> Homo sapien</pre>	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag	120 180 240 300 360
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgt cctgatgcag ccacagcagc ccgaaggg tggatgttgt tggtgatggt ggagatga gcatggtggt cggctttyar carccggg tggtggatct nggatgttgg aattctgg cagctcatca gtcaggactc gcctgccc ctcaatgttt gacattgctg gaccaggg <210> 12 <211> 560 <212> DNA <213> Homo sapien <400> 12</pre>	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt cac catatggtaa gga gttccagcac	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc ttctangang	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag a	120 180 240 300 360 411
<pre><221> misc_feature <222> (1)(411) <223> n = A,T,C or G <400> 11 tcctcattgg tcggggccaa aagcgtgtcctgatgcag ccacagcagc ccgaagggtggatgttgt tggtgatggt ggagatgatggtggtggtcatcatca ggcttyar carccgggtggtggatct nggatgttgg aattctggcagctcatca gtcaggactc gcctgccctcaatgtt gacattgctg gaccaggg <210> 12 <211> 560 <212> DNA <213> Homo sapien <400> 12 tacttgcctg gagatwgcyt tykøkwere</pre>	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt cac catatggtaa gga gttccagcac atg, ytcwrawgtc	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc ttctangang cgtggataca	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag a	120 180 240 300 360 411
<pre><221> misc_feature</pre>	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt cac catatggtaa gga gttccagcac mtg ytcwrawgtc agg acaagcctgt	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc ttctangang cgtggataca aacgaatagt	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag a gaaatctctgz	120 180 240 300 360 411
<221> misc_feature	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa gga gttccagcac atg. ytcwrawgtc agg acaagcctgt aat ggcaggtgtg	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc ttctangang cgtggataca aacgaatagt agtgcctgta	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag a gaaatctctg2	120 180 240 300 360 411
<pre><221> misc_feature</pre>	gtc tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa gga gttccagcac atg. ytcwrawgtc agg acaagctgt aat ggcaggtgtg gct atgtggtatc	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc ttctangang cgtggataca aacgaatagt agtgcctgta ttgatcctag	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag a gaaatctctga	120 180 240 300 360 411
<221> misc_feature	tcaaaggtgt acc ttatcgatga gca cagttcacag gta catagnaggt acc catatggtaa gga gttccagcac atg. ytcwrawgtc agg acaagctgt aat ggcaggtgtg gct atgtggtatc agc aattttggt	cctcgatctc ggtgcaccac ttacaatccc gaggggtcat gcsgragggc ttctangang cgtggataca aacgaatagt agtgcctgta ttgatcctag tctgaagatg	aatgatctgc cccgttggtt attaggatag gcccgtgttt atttgagcag a gaaatctctg taaattcacg taaaatattc cattagcaat taggctctag	120 180 240 300 360 411

·42.

```
cttgcttctg atcctgctcc tgcaggtggg cgacaggtat cctaggagct gttttcaaat
                                                                        480
ctaagtctga tcgcattgtg aatgaaactc tctatgaaaa cacaaagctt ttgaqcqcca
                                                                        540
caggggaaag tgaaaaacaa
                                                                        560
      <210> 13
      <211> 150
      <212> DNA
      <213> Homo sapien
      <400> 13
gggcaggctg tctttttaaa atgtctcggc tagctagacc acagatatct tctagacata
                                                                        60
ttgaacacat ttaagatttg agggatataa gggaaaatga tatgaatgtg tatttttact
                                                                        120
caaaataaaa gtaactgttt acgttggtga
                                                                        150
      <210> 14
      <211> 403
      <212> DNA
      <213> Homo sapien
      <400> 14
ctgctgcctg tggcgtgtgt gggctggatc ccttgaaggc tgagtttttg agggcagaaa
                                                                        60
gctagctatg ggtagccagg tgttacaaag gtgctgctcc ttctccaacc cctacttggt
                                                                       120
ttccctcacc ccaagcctca tgttcatacc agccagtggg ttcagcagaa cgcatgacac
                                                                       180
cttatcacct ccctccttgg gtgagctctg aacaccagct ttggcccctc cacagtaagg
                                                                       240
ctgctacatc aggggcaacc ctggctctat cattttcctt ttttgccaaa aggaccagta
                                                                       300
gcataggtga gccctgagca ctaaaaggag gggtccctga agctttccca ctatagtgtg
                                                                       360
gagttctgtc cctgaggtgg gtacagcagc cttggttcct ctg
                                                                       403
      <210> 15
      <211> 688
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(688)
      \langle 223 \rangle n = A,T,C or G
      <400> 15
caaagcacat tttaatcatt tattttaaaa gggggagtaa agcatttaaa ctgccaatcc
                                                                        60
tatagactag gacttgaaca tcaaaggaaa aatagacaaa gactagatga taaagtcatt
                                                                       120
caaaagcaca gaagcacatc acatacacca gcaaggtttc caactactgc actgattaac
                                                                       180
tagatactct caatagcttt tctatagctc gtcctagaaa aaaaaattaa attttcattt
                                                                       240
tcttacaagt tccaggctta aacaaaggca aaaattacat gcaacaactg atacactcat
                                                                       300
aagttgcaca tatgctccaa ggtctttatt agataacaat aaatgctagc actttgtcac
                                                                       360
tgccatcaga ttttccttat agtcttagag tcatgtaaat aaaagttcca taatgaaatt
                                                                       420
aaagaaaatt aatttttcta atcttagatc agttccatag aaaactatta atttttttaa
                                                                       480
agtaggcagt agaagggggt tgggaggg tggaattggt tagtaagtct ggttctaatc
                                                                       540
ttctgagctg cctttggaag gaagttatga ggtagaagat tctactgact tttagtaagg
                                                                       600
tggacaatga gagaaaagaa aaagcaggtg cctcatcnnc agatccttnt ggtatttatn
                                                                       660
tgccangtnc nanntaatnc atanaaag
                                                                       688
      <210> 16
      <211> 408
```

<212> DNA

<400> 16

```
<213> Homo sapien
```

```
caggicatca agaigactta caggaigtaa tagggagagc tgicgagait ggigitaaaa
                                                                         60
 agtttatgat tacaggtgga aatctacaag acagtaaaga tgcactgcat ttggcacaaa
                                                                        120
 caaatggtat gtttttcagt acagttggat gtcgtcctac aagatgtggt gaatttgaaa
                                                                        180
 agaataaccc tgatctttac ttaaaggagt tgctaaatct tgctgaaaac aataaaggga
                                                                        240
 aagttgtggc aataggagaa tgcggacttg attttgaccc gactgcagtt ttgtcccaaa
                                                                        300
gatactcaac tcaaatattt tgaaaaacag tttgaactgt cagaacaaac aaaattacca
                                                                        360
 atgtttcttc attgtccgaa actcacatgc tgaatttttg gacataat
                                                                        408
       <210> 17
       <211> 407
       <212> DNA
       <213>Homo-sapien
       <400> 17
ggtcctgggg aggccctagg ggagcaccgt gatggagagg acagagcagg ggctccagca
                                                                        60
ccttctttct ggactggcgt tcacctccct gctcagtgct tgggctccac gggcaggggt
                                                                       120
cagagcactc cctaatttat gtgctatata aatatgtcag atgtacatag agatctattt
                                                                       180
tttctaaaac attcccctyc ccactcctct cccacagagt gctggactgt tccaggccct
                                                                       240
ccagtgggct gatgctggga cccttaggat ggggctccca gctcctttct cctgtgaatg
                                                                       300
gaggcagaag acctccaata aagtgccttc tgggcttttt ctaacctttg tcttagctac
                                                                       360
ctgtgtactg aaatttgggc ctttggatcg aatatggtca agaggtt
                                                                       407
      <210> 18
      <211> 405
      <212> DNA
      <213> Homo sapien
      <400> 18
tgaagagtca acttgggcct ggaggactga taaagtttgt gattttgagg gcctctaaaa
                                                                        60
gtattaaagc agcggcagcc gctgcacgca gacatgaggg ctaggttaaa acagtaagat
                                                                       120
caagttgttt ggacagaaag gctacagagt gtggtcctgg ctcttgtgta agaattacga
                                                                       180
ccacgctaac catgcctagg aaggaaagga gttattgttt tgtagaaagg tgctggggtt
                                                                       240
tgagagatca gtcggacacg attggcaggg agagcacgtg tgtttttatg agaattatgc
                                                                       300
ccgagatagg taacagatga ggaagaaatt tgggcttgat tgaagtaatg ggggctgtct
                                                                       360
gtgaagettt geageagtae ageetaggta atttgetgag eetaa
                                                                       405
      <210> 19
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 19
tcctgacatt cctgccttct tatattaata agacaaataa aacaaaatag tgttgaagtg
                                                                        60
ttggggcagc gaaaattttt ggggggtggt atggagagat aatgggcgat gtttctcagg
                                                                       120
gctgcttcaa gcgggattag gggcggcgtg ggagcctaga gtgggagaga ttaagctgaa
                                                                      180
gggaggtctt gtggtaaggg gtgatatcat ggggatgtta gaagaaacat ttgtcgtata
                                                                      240
gaatgattgg tgatggcctg gatacggttt tggatgattt gagaagctaa atggaagata
                                                                      300
caaggtccga ataaaaggag gagaaaaatg ggtattaaat gtctaagaat tgggaggacc
                                                                      360
taggacatct gattagagag tgcctaagga gattcagcat a
                                                                      401
      <210> 20
```

<211> 331

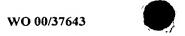
```
<212> DNA
      <213> Homo sapien
      <400> 20
aggtccagct ctgtctcata cttgactcta aagtcatcag cagcaagacg ggcattgtca
                                                                        60
atctgcagaa cgatgcgggc attgtccaca gtatttgcga agatctgagc cctcaggtcc
                                                                       120
tcgatgatct tgaagtaatg gctccagtct ctgacctggg gtcccttctt ctccaagtgc
                                                                       180
teceggattt tgeteteeag ceteeggtte teggteteea ggeteeteac tetgteeagg
                                                                       240
taagaggcca ggcggtcgtt caggctttgc atggtctcct tctcgttctg gatgcctccc
                                                                       300
attcctgcca gacccccggc tatcccggtg g
                                                                       331
      <210> 21
      <211> 346
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(346)
      <223> n = A,T,C or G
      <400> 21
ggtccaccac ttgtacccga tatggacttc cggcttctct gtccaatgga gccacactaa
                                                                       60
agateteace agteaegtgg teaattttaa gecaacetet tgtgteteee eteagtgaat
                                                                       120
agcttatgtc cagaccttct ggatccttgg cagtcacatt gcccacttta gtgcctatag
                                                                       180
ctacatcctc actgactttc gcttggaata cgtgttggga aaattgaggt gcttcattca
                                                                       240
catctgtcac aataagncgt gaacttggca aaagaacttg cattgtactt cacaccaaac
                                                                      300
actagaggct caggattttc tgctttgaac acaatgttgg aaacag
                                                                       346
     <210> 22
      <211> 360
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
     <222> (1)...(360)
      <223> n = A,T,C or G
      <400> 22
gaagactccc tctctcggaa gccggatccc gagccgggca ggatggatca ccaccagccg
                                                                       60
gggactgggc gctaccaggt gcttcttaat gaagaggata actcagaatc atcggctata
                                                                      120
gagcagccac ctacttcaaa cccagcaccc gcagattgtg caggctgcgt cttcagcacc
                                                                      180
agcacttgaa actgactctt cccctccacc atatagtagt attactggtg gaagtaccta
                                                                      240
caacttcaga tacagaagtt tacggtgagt tttatcccgt gccacctccc tatagcgttg
                                                                      300
ctacctctct tcctacnwta cgatgaaagc tgagaaggct aaagctgctg caatggcatg
                                                                      360
      <210> 23
      <211> 251
      <212> DNA
      <213> Homo sapien
      <400> 23
ggcggagctc cacgacgagc tggaaaagga accttttgag gatggctttg caaatgggga
                                                                       60
agaaagtact ccaaccagag atgctgtggt cacgtatact gcagaaagta aaggagtcgt
                                                                      120
```



```
gaagtttggc tggatcaagg gtgtattagt acgttgtatg ttaaacattt ggggtgtgat
                                                                                                                                                                  180
  gcttttcatt agattgtcat ggattgtggg tcaagctgga ataggtctat cagtccttgt
                                                                                                                                                                  240
   aataatgatg g
                                                                                                                                                                  251
                <210> 24
                <211> 421
                <212> DNA
                <213> Homo sapien
               <220>
               <221> misc_feature
               <222> (1)...(421)
               \langle 223 \rangle n = A,T,C or G
2.45 cm = 2.45 cm = 1.55 c
 caggitette ccaggigitg actecagete cagetteage tecageteca ggieggete
                                                                                                                                                                   60
 cagetecage egeagettar geagegggag gttetgtgte eeagttgttt tecaatttea
                                                                                                                                                                 120
 ccggctcccg tggatgamcg ygggacctgy caswgctcct gtktycctgc yagsacacca
                                                                                                                                                                 180
 cnytttyccg tggacacrar kggaacckct tggaattcac agctyatgtt ctttctcara
                                                                                                                                                                 240
 agtttgagaa agaactttct aaagtgaggg aatatgtcca attaattagt gtgtatgaaa
                                                                                                                                                                 300
 agaaactgtt aaacctaact gtccgaattg acatcatgga raaaggatac catttcttac
                                                                                                                                                                360
 actgaactgg acttcgagct gatcaaggta gaagtgaagg agatggaaaa actggtcata
                                                                                                                                                               420
                                                                                                                                                                 421
               <210> 25
               <211> 381
               <212> DNA
               <213> Homo sapien
               <220>
               <221> misc_feature
               <222> (1)...(381)
              \langle 223 \rangle n = A,T,C or G
               <400> 25
gaactttttg tttctttatt ttcaatattt gtcttattaa tatttttctt attttataat
                                                                                                                                                                 60
gcaattacaa caatttagga nacaaaacaa tataaacaaa agaatgttaa atagttttt
                                                                                                                                                               120
ttaaaaaata gcttgttgct tgcaanaaag tccatataat cttattcccc cccaaatata
                                                                                                                                                               180
attttatact ttgcactaaa ccaaaatagc ttatggaaaa ttagtattaa atagctaaac
                                                                                                                                                               240
acagaaaacc tacagctata aataacataa aatacagttt aactttaatg ngatgcttaa
                                                                                                                                                               300
acaaagcaaa ctatgatgca atatgaatca acttcattaa ttggacaagt ccagnggagg
                                                                                                                                                               360
 cacaaattag ataagcacta a
                                                                                                                                                               381
              <210> 26
              <211> 401
              <212> DNA
              <213> Homo sapien
              <220>
              <221> misc_feature
              <222> (1)...(401)
              <223> n = A, T, C or G
              <400> 26
ggaaaaggga ctggcctctc tgaagagtga gatgagggaa gtggaaggag agctggaaag
```

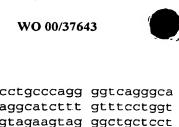
```
gaaggagctg gagtttgaca cgaatatgga tgcagtacag atggtgatta cagaagccca
                                                                        120
qaaggttgat accagaagcc aagaacgctg gggttacaat ccaagacaca ctcaacacat
                                                                        180
tagacgggct cctgcattct gatggaccaa ccttttcang tggtaagatt gaagangggg
                                                                        240
cctqqqctta cctqqqaagc aaaaactttt cccqanccaa ggaacccagg attcaaccan
                                                                        300
gcnacttgcn ggccaaggaa ggcanaactn ggaanaaaag gccccttaag caaaagggnc
                                                                        360
accttcattt gctnggaaan cagcctttan ttggaatctt g
                                                                        401
      <210> 27
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (383)
      \langle 223 \rangle n = A,T,C or G
      <400> 27
aattgcaact ggacttttat tgggcagtta cnacaacnaa tgttttcana aaaatatttg
                                                                         60
gaaaaaatat accacttcat agctaagtct tacagagaan aggatttgct aataaaactt
                                                                        120
aagttttgaa aattaagatg cnggtanagc ttctgaacta atgcccacag ctccaaggaa
                                                                        180
nacatgtcct attragttat tcaaatacca gtrgagggca ttgtgattaa gcaaacaata
                                                                        240
tatttgttan aactttgntt ttaaattact gntnettgae attacttata aaggagnete
                                                                        300
taactttcga tttctaaaac tatgtaatac aaaagtatan ntttccccat tttgataaaa
                                                                        360
gggccnanga tactgantag gaa
                                                                        383
      <210> 28
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(401)
      <223> n = A, T, C \text{ or } G
      <400> 28
ggtcgcgttt cccctggctc acagtctgcc attatttgca tttttaaatg aagaaaagtt
                                                                         60
taacgtggat ggatggacag tttacaatcc agtggaagaa tacaggaggc agggcttgcc
                                                                        120
caatcaccat tggagaataa cttttattaa taagtgctat gagctctgcg acacttaccc
                                                                        180
tgctcttttg gtggttccgt atcgtgcctc anatgatgac ctccggagag ttgcaacttt
                                                                        240
taggtcccga aatcgaattc cagtgctgtc atggattcat ccagaaaaata agacggtcat
                                                                        300
tgtgcgttgc agtcagcctc ttgtcggtat gagtgggaaa cgaaataaag atgatgagaa
                                                                        360
atatctcgat gttatcaggg agactaataa acaaatttct a
                                                                        401
      <210> 29
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 29
atatgagttt gccatctcca tggatgccat ttcaatgcct tcagggtaat cattctctcc
                                                                         60
ccaaagactg cccacggggt catcactcct gtgacgaaat gagggctgga ttgaagatgt
                                                                        120
tctgctgagc accccctgg tcatctttgg ggtctcagaa gagccataat catgaccatt
                                                                        180
ctcagcatct gaataatcag gttctctcca agtgcttggc aagttctgat tgtcctcagc
                                                                        240
```

actgggatag tctggctcc caaaaaaggg tggagagtta ggttgaatgt cagcgcctgg ataatcaggc tttcccagag agtctgcgta tggattgatt ctaaaacttg tatgttccag attcttctg gatcctggat ggttcaaatt ggctctgggt c	300 360 401
(21) Nomo Bupien	
<pre><400> 30 Cctgaactat ttattaaaaa catgaccact cttggctatt gaagatgctg cctgtatttg agagactgcc atacataata tatgacttcc tagggatctg aaatccataa actaagagaa actgtgtata gcttacctga acaggaatcc ttactgatat ttatagaaca gttgatttcc cccatcccca gtttatggat atgctgcttt aaacttggaa gggggagaca ggaagtttta attgttctga ctaaacttag gagttgagct aggagtgcgt tcatggttc ttcactaaca gaggaattat gctttgcact acgtccctcc aagtgaagac agactgtttt agacagactt tttaaaaatgg tgccctacca ttgacacatg cagaaattgg t</pre>	60 120 180 240 300 360 401
<210> 31 <211> 297 <212> DNA <213> Homo sapien	
<400> 31	
acctccatta atgccaggtg ttcctcctct gatgccagga atgccaccag ttatgccagg catgccacct ggattgcatc atcagagaaa atacacccag tcattttgcg gtgaaaacat aatgatgcca atgggtggaa tgatgccacc tggaccagga ataccacctc tgatgcctgg aatgccacca ggtatgcccc cacctgttcc acgtcctgga attcctcaa tgactcaagc acaggctgtt tcagcgccag gtattcttaa tagaccacct gcaccaacag caactgt	60 120 180 240 297
<211> 401	
<212> DNA	
<213> Homo sapien	
<pre><400> 32 caaacctgga gccaaaaagg acacaaagga ctctcgaccc aaactgccc agacctctc cagaggttgg ggtgaccaac tcatctggac tcagacatat gaagaagctc tatataaatc caagacaagc aacaaaccct tgatgattat tcatcacttg ggtgagtgcc cacacagtca agctttaaag aaagtgtttg ctgaaaataa agaaatccag aaattggcag agcagtttgt cctcctcaat ctggtttatg aacaactga caaacacctt tctcctgatg gccagtatgt ccccaggatt atgtttgttg acccatctct gacagttaga gcccgatatc actggaagat attcaaaccg tctctatgct tacgaacctg cagatacagc t</pre>	60 120 180 240 300 360 401
<210> 33 <211> 401 <212> DNA <213> Homo sapien	-
<400> 33	
agcagaggga caggaatcat tcggccactg ttcagacggg agccacaccc ttctccaatc caagcctggc cccagaagat cacaaagagc caaagaaact ggcaggtgtc cacgcgctcc aggccagtga gttggttgtc acttactttt tctgtgggga agaaattcca taccggagga tgctgaaggc tcagagcttg accctgggcc actttaaaga gcagctcagc aaaaagggaa attataggta ttacttcaaa aaagcaagcg atgagtttgc ctgtggagcg gtgtttgagg	60 120 180 240 300



agatetggga ggatgagaeg gtgeteeega t ageggatega ttgageeetg gggtetgget t			ggcaaagtgg	360 401
<210> 34 <211> 401 <212> DNA <213> Homo sapien				
<pre><400> 34 aacaatggct atgaaggcat tgtcgttgca a ctcattcaac aaataaagga catggtgacc c ggaaagcgat tttatttcaa aaatgttgcc a gctgactatg tgagaccaaa acttgagacc t gtctactcct ccaggtaatg atgaacccta c aggggtgaaa ggatcccacc tcactcctga t atggaccaca aggtaagggc atttgtccat g</pre>	caggcatctc attttgattc tacaaaaatg cactgagcag tttcattgca	tgtatctgtt ctgaaacatg ctgatgttct atggggcaac ggaaaaaagt	tgaagctaca gaagacaaag ggttgcttga tgtggagaga	60 120 180 240 300 360 401
<210> 35 <211> 401 <212> DNA <213> Homo sapien				
<220> <221> misc_feature <222> (1)(401) <223> n = A,T,C or G				
<pre><400> 35 catttettee tactagactg ceeecttgat of ctteaggtgg tgeteettea ttattecaag g gggtaaagee tttggegeee ttteegeaat g geangaacag aaagggeaaa ateatganeg of aateatgetg ngetteeetg cancegetge of aggacetget ttteaggaca actaaaacce t ctteteecaa getttttete aetttggtge of</pre>	gatgcagcat ggcacatcag caattgctgc catgcaagac tgattgnctg	ctctatggtg cagtaaaagt gggtcccaag actnacaaac aaatcaggaa	ccaggtatgg ggtaccaata cccacatagg tgngantgta	60 120 180 240 300 360 401
<210> 36 <211> 401 <212> DNA <213> Homo sapien				
<pre><400> 36 cctgctagaa tcactgccgc tgtgctttcg t tctgtttttg ttttacatta gtcattggac d acaaagaaat gaacagttgt agggagaccc a ttgaagttcg ggtttttgtg ttaagttaat d actatacatc tgtatatagt gtacggcaaa a actttaaatc agtacagtac ctgtacctgc a ttgagggctc aagctttccc ttgttttttg a</pre>	cacagccatt agcagcacct ctgtacattc agagtattaa acggtcaccc	caggaactac ttcctccaca tgtttgccat tccactatct gctccgtgtg	cccctgccc caccttcatt tgttacttgt ctagtgcttg tcgccctata	60 120 180 240 300 360 401
<210> 37 <211> 401 <212> DNA <213> Homo sapien				

```
<220>
       <221> misc_feature
       <222> (1)...(401)
       <223> n = A, T, C \text{ or } G
       <400> 37
 cnnctntgna atggantnnt tgnctaaaan ganttgatga tgatgaanat ccctangang
                                                                         60
 antaagcatg gancntgatc ntttnctnng cactccttta cgacacggaa acangnatca
                                                                        120
ncatgatggt accaganacc ttatcaccna cgcgcacnga nctgactnat tccaaagagt
                                                                        180
 tgnggttacg gncatccggt cattgctcgt gcccattgct gcagggctga tnctactggt
                                                                        240
gettattatg ntggeeetga ggatgeteea caatgaatat aageatgetg catgateage
                                                                        300
ggcaacanat gctctgccgt ttgcactaca tctttcacgg acacnatntc gaanacgggc
                                                                        360
 acnttgcana gttagacttg gaatgcatgg ngccggncan n
                                                                        401
 <211> 401
       <212> DNA
       <213> Homo sapien
       <400> 38
aattggctca ctctctcaag gcaagcactg tctcaaggca gtctcaaggc agagatgaca
                                                                        60
cagcaaaaaa cagagggga gaaaaaagtc tattattggc ttgtgattta caaaagccaa
                                                                       120
agtcctttag ataaaaggcc aggagtcgta ccaacataga taccaaatcc aggagaacac
                                                                       180
agaccagega taagagggac getteeceat gacccagace agectaaage eeetgtgggg
                                                                       240
gcagccagtg gggagctgtc agaccttgga catggtggtc tttgagaatg ggtctgccct
                                                                       300
teteteetg accagttggg atagacacet gactggaate ettgacactg geaggtgttt
                                                                       360
ctatgaacag agaggactgt gcctgtcttc ctgaatccca a
                                                                       401
      <210> 39
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(401)
      <223> n = A, T, C \text{ or } G
      <400> 39
tctggtangg agcaattcta ttatttggca ttgcatggct gggttgaatt aaaacaggga
                                                                        60
gtgagaacag gtgagtctag aagtccaact ctgaaaagga ccactgtaca tttgaacaca
                                                                       120
cggctgtgtt aaagatgctg ctaatgtcag tcactgggtg cactaaagga tctcttattt
                                                                       180
tatgtaaaac gttgggaatg acaagatana actgatactc tggtaagtta ccctctgaag
                                                                       240
ctacttcttg tgaaatacta atgacagcat catcctgcca agcgaaagag gcaggcataa
                                                                       300
gcaaggacaa attaaaaggg ggtaagagcc ttatcatgat gaggagtctt gttttgacat
                                                                       360
cttgggaaaa gctgtccata gtgtgaagtc gtcaatttct c
                                                                       401
      <210> 40
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 40
tctggtcacc caactcttgt ggaagagggg aattgagatc gagtactgaa tatctggcag
                                                                       60
agaggctgga atccttcagc cccagagccc agggaccact ccagtagatg cagagagggg
                                                                      120
```



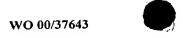
```
cctgcccagg ggtcagggca gtgggtatca ctggtgacat caagaatatc agggctgggg
                                                                        180
aggcatcttt gtttcctggt gccctcctca aagttgctga cactttgggg acgggaaggg
                                                                        240
gtagaagtag ggctgctcct tttggagctg gagggaatag acctggagac agagttgagg
                                                                        300
cagtcgggct gtccaggttc taagcatcac agcttctgca ctgggctctg aggagattct
                                                                        360
cagccagagg atcccagcct cctcctcct caaatgtcaa g
                                                                        401
      <210> 41
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(401)
      \langle 223 \rangle n = A,T,C or G
      <400> 41
ctggactaaa aatgtccact atggggtgca ctctacagtt tttgaaatgc taggaggcag
                                                                         60
aaggggcaga gagtaaaaaa catgacctgg tagaaggaag agaggcaaag gaaactaggt
                                                                        120
ggggaggate aattagagag gaggeacetg ggateeacet tetteettan gteeceteet
                                                                        180
ccatcagcaa aggagcactt ctctaatcat gccctcccga agactggctg ggagaaggtt
                                                                        240
taaaaacaaa aaatccagga gtaagagcct taggtcagtt tgaaattgga gacaaactgt
                                                                        300
ctggcaaagg gtgcganagg gagettgtge teangagtee ageeegteea geeteggggt
                                                                        360
gtangtttct gaagtgtgcc attggggcct caccttctct q
                                                                        401
      <210> 42
      <211> 310
      <212> DNA
      <213> Homo sapien
      <400> 42
ggttcgacaa atccccaaaa atggcaaatt aagccctgtg acaaaataag ttattggatc
                                                                        60
atacagaaat agcccaaatc tggaaatttt gaattaaaat tgtaatcctg taaaacaagt
                                                                       120
tttggggtga atggatttct ttaataccaa taatatttt aattcccacc acagatggat
                                                                       180
ttgctgaata tgctaatgct gtgaatgaga aaacaatttt ggggtaggta tacccacaag
                                                                       240
taatctgatg acaaaataaa ccacagactg atgtcaaatg gacaaaaaac tgaaaatatg
                                                                       300
ctgtgagaaa
                                                                       310
      <210> 43
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 43
aggicactia cactigigac cagigigggg cagagaccia ccagccgatc cagiciccca
                                                                        60
ctttcatgcc tctgatcatg tgcccaagcc aggagtgcca aaccaaccgc tcaggagggc
                                                                       120
ggctgtatct gcagacacgg ggctccagat tcatcaaatt ccaggagatg aagatgcaag
                                                                       180
aacatagtga tcaggtgcct gtgggaaata tccctcgtag tatcacggtg ctggtagaag
                                                                       240
gagagaacac aaggattgcc cagcctggag accacgtcag egtcactggt attttcttgc
                                                                       300
caatcetgeg cactgggtte egacaggtgg tacagggttt acteteagaa acetacetgg
                                                                       360
aagcccatcg gattgtgaag atgaacaaga gtgaggatga t
                                                                       401
      <210> 44
      <211> 401
      <212> DNA
```

```
14
       <213> Homo sapien
       <400> 44
 atccctgtaa gtctattaaa tgtaaataat acatacttta caacttctct tagtcggccc
                                                                          60
 ttggcagatt aaatctttgc aaaattccat atgtgctatt gaaaaatgaa ataaaacctc
                                                                         120
 agatgtctga attcttattt caaatacagt tatataatta ttttaaatta caatatacaa
                                                                         180
 tttctgttaa atacaactgt taagggattc tgagaacaat tataagatta taataatata
                                                                         240
 tacaaactaa cttctgaaat gacatgggtt gtttccttcc caccctccta ccctctcaaa
                                                                         300
gagtttttgc atttgctgtt cctggttgca aaaggcaaaa gaaaatctaa aaatagtctg
                                                                         360
 tgtgtgtcca cgacatgctc gctcctttga gaatctcaaa c
                                                                         401
       <210> 45
       <211> 401
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(401)
       <223> n = A,T,C or G
      <400> 45
gtgcctgctg cctggcagcc tggccctgcc gctgcctcag gaggcgggag gcatgagtga
                                                                         60
gctacagtgg gaacaggctc aggactatct caagagattt tatctctatg actcagaaac
                                                                        120
aaaaaatgcc aacagtttag aagccaaact caaggagatg caaaaaattc tttggcctac
                                                                        180
ctatactgga atggtaaact cccgcgtcat anaaataatg caanaagccc agatgtggag
                                                                        240
tgccagatgt tgcagaatac tcactatttc caaatagccc aaaatggact tccaaagtgg
                                                                        300
tcacctacag gatcgtatca tatactcgag acttaccgca tattacagtg gatcgattag
                                                                        360
tgtcaaaggc tttaaacatg tggggcaaag agatccccct g
                                                                        401
      <210> 46
      <211> 401
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(401)
      <223> n = A, T, C \text{ or } G
      <400> 46
gtcagaattg tctttctgaa aggaagcact cggaatcctt ccgaactttc caagtccatc
                                                                        60
catgattcan agatactgcc ttctctctc ctgggatttt atgtgtttct gatagtgaat
                                                                        120
tgttgatgta tttgctactt tgcttctttt ctctttcaag acttgatcat tttatatgct
                                                                       180
gnttggagaa aaaaagaact tttggtagca aggaggtttc aagaaatgat tttggatttt
                                                                       240
ctgctgcgga atttctcggc acctacctgt agtatggggc acttggtttg gttgcagagt
                                                                       300
aagaaggtgg aagaatgagc tgtacttggt taagcagttg aaaccttttt tgagcaggat
                                                                       360
ctgtaaaagc ataattgaat ttgtttcacc cccgtggatt c
                                                                       401
      <210> 47
      <211> 401
```

<400> 47

<212> DNA

<213> Homo sapien



```
ggtctgcagc aatgcacttc aaccatacat actgcttcca ctagctaata ccaaatgcag
                                                                         60
gttctcagat ccagacaaat ggaggaaaag aacatttatg cttccgtttc agaaagccaa
                                                                        120
qtcgtagttt tggcccttcc tttctctaaa gtttattccc aaaaacaggt agcattcctg
                                                                        180
artgggcaga gaagaggata ttttcagccc acatctgctg caggtatgtc attttctccc
                                                                        240
atcttcactg tgactagtaa agatctcacc acttctcttt ggaatttcca actttgcttg
                                                                        300
tgattgaatg tcacttcgtg aatttgtatt atgtcagatc acttggcatt gctcttccat
                                                                        360
                                                                        401
atgcatcaag ttgccaggca ctaaacccaa tgttcatgaa c
      <210> 48
      <211> 430
      <212> DNA
      <213> Homo sapien
      <400> 48
acataacttg taaacttttt ctgcttgggg gctgtaacag acagaagagt aaagactaca
                                                                         60
aggattttct gaagatgctt caatgaaaat catcatttcc tctttagtca tcccaagtct
                                                                        120
tggtttgaaa aacttgggca tggacttata cagaccttga accaccactg acttatcatt
                                                                        180
gggtggcaga ccttgaaacc aagctctctg tgttacttct gaaagtgcat caattctgat
                                                                        240
ttggctaaga acagaagaca aatactggga tcgtgattct gtgttatact ctagccacag
                                                                        300
catagoagor totogaacgo tttottoott ttotacattt aaattgtoac tactgagaat
                                                                        360
                                                                        420
atctatcagt aggicatgig acagaccigc cccggggccg gcccgcicga tgctigccga
                                                                        430
atatcatqqt
      <210> 49
      <211> 57
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(57)
      \langle 223 \rangle n = A,T,C or G
      <400> 49
ggtattaaca atatcangca ctcattcttc ccctcttatg aaanggatna attttta
                                                                         57
      <210> 50
      <211> 327
       <212> DNA
      <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(327)
       <223> n = A, T, C or G
       <400> 50
gatggnggtn tccacaagan tnaangtncn tattaantan nncttgtaga nccacttnna
                                                                         60
ttaattgnnn tatgnntgnc cttctggtgg ntgtngaagc ttcatatnnt ntttggacat
                                                                        120
cattacacgt cttagctctt tnaagnacaa ctttaatgct atatgaattt tgccattttn
                                                                        180
                                                                        240
gctaacactg gtatgctccn ngcatccacc atnccacntg gaattattta ttncnttcat
attaatnttt tgtttaccaa atctnacttg acccgaacga aactttctgn gtattttang
                                                                        300
                                                                        327
gccccnccat tcttactttt caagcct
```

<210> 51

```
<211> 236
      <212> DNA
      <213> Homo sapien
      <400> 51
cgtctcgaag aagcgctgca ggccgatgat ggactgcacg tctgccttgt cctcagttaa
                                                                         60
cttgttgaat tgcttgaaca tgcggcccac atcctgggca aactcctgtg gggagctgta
                                                                         120
gggaggtgac aactteteet ggaggeggge aeggateagg gteagateea gggtgeeace
                                                                         180
gggctggtcc agggagaagg tggagtcgta gccagacctg cccgggcggc cgctcq
                                                                         236
      <210> 52
      <211> 291
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(291)
      \langle 223 \rangle n = A,T,C or G
      <400> 52
ctcacatcct gggtccggct gtagagctgc accatggtgc tgagcgcccc ctccagctcc
                                                                         60
ttgtagatgt aaaggacggc gaaggagctg tagtctgtgt ccacgatgcg cacgtccagg
                                                                        120
tagcccaagg cogggactot gaagttgtoo ctoggagcoc accttcangt actogggcat
                                                                        180
ccacctggtt acagcenttc gncctcggna actccatntg gactttacag gccgcctcc
                                                                        240
tetgtgggee tgatggmeet tgeaggacat mggaacaegg gagetemett t
                                                                        291
      <210> 53
      <211> 95
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(95)
      <223> n = A,T,C \text{ or } G
      <400> 53
gtctgtgcag tttctgacac ttgttgttga acatggntaa atacaatggg tatcgctgan
                                                                         60
cactaagttg tanaanttaa caaatgtgct gnttg
                                                                         95
      <210> 54
      <211> 66
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (66)"
      <223> n = A,T,C or G
      <400> 54
cctnaatnat ntnaatggta tcaatnnccc tgaangangg gancggngga agccggnttt
                                                                         60
gtccgg
                                                                         66
```



```
<210> 55
              <211> 265
              <212> DNA
              <213> Homo sapien
              <220>
              <221> misc_feature
              <222> (1)...(265)
              <223> n = A, T, C or G
              <400> 55
atctttcttc tcagtgcctt ggccntgttg agtctatctg gtaacactgg agctgactcc
                                                                                                                                                                     60
ctgggaagag aggccaaatg ttacaatgaa cttaatggat gcaccaagat atatgacct
                                                                                                                                                                   120
gtctgtggga ctgatggaaa tacttatccc aatgaatgcc gtgttatgtt tttgaaaatc
                                                                                                                                                                   180
ggaaacgcca gacttctatc ctcattcaaa aatctgggcc ttmctgaaaa ccagggtttt
                                                                                                                                                                   240
naaaatccca ttcnggtcnc cggcg
                                                                                                                                                                   265
              <210> 56
              <211> 420
              <212> DNA
              <213> Homo sapien
              <220>
              <221> misc_feature
              <222> (1)...(420)
              \langle 223 \rangle n = A,T,C or G
              <400> 56
gageggeege cegggeaggt cetegeggtg acctgatggg attteaaaac ettggttete
                                                                                                                                                                     60
agcaaggccc agatttttga atgangatag aagtctggcg tttccgattt tcaaaacata
                                                                                                                                                                   120
acacgcatte attgggataa gtatttecat cagteecaca gaengggtea tatatettgg
                                                                                                                                                                   180
gtgCatccat taagttcntt tgttaacatt tgggcctctc tttcccangg gaattcaget
                                                                                                                                                                   240
cccagttgtt taccaanatt naactccacc ggggccaaag gcncttgaaa aaaaaaanaa
                                                                                                                                                                   300
ttccttgttt accttccttg ggcttnaagt tctggcgtcc aaaagttcaa tttgaaaact
                                                                                                                                                                   360
gcaccgcact taccacgtct cttcnagaan cctggggaca cctcggccgc gaccacgcta
                                                                                                                                                                   420
              <210> 57
              <211> 170
              <212> DNA
              <213> Homo sapien
              <400> 57
gaagcggagt tgcagcgct ggtggccgcc gagcagcaga aggcgcagtt tactgcacag
                                                                                                                                                                    60
gtgcatcact tcatggagtt atgttgggat aaatgtgtgg agaagccagg gaatcgccta
                                                                                                                                                                  120
gactetegea etgaaaattg teteteeaga eeteggeege gaceaegeta
                                                                                                                                                                  170
              <210> 58
              <211> 193
              <212> DNA
              <213> Homo sapien
              <400> 58
attiticaging changement of the state of the 
                                                                                                                                                                    60
ctccatgaag tgatgcacct gtgcagtaaa ctgcgccttc tgctgctcgg cggccaccag
                                                                                                                                                                  120
gcgctgcaac tccgcttcat cggcttcgcc cagctccgcc attgttcgcc acctgcccgg
                                                                                                                                                                  180
```

```
gcggccgctc gaa
                                                                      193
      <210> 59
       <211> 229
       <212> DNA
       <213> Homo sapien
      <400> 59
cgcaactctc gagcatttat atacaatagc aaatcatcca gtgtgttgta cagtctataa
                                                                       60
tactccaaca gtctcccatc tgtattcaat ggcgccaccc aatacagtcc tttgtttgga
                                                                      120
tgctggggag agtaatccct accccaagca ccatatagat aagaaaaccc tctccagttg
                                                                      180
agctgaacca cagacggttt gctgatacct gcccgggcgg ccgctcgaa
                                                                      229
     <210> 50
 <212> DNA
      <213> Homo sapien
      <400> 50
tegageggee geeegggeag gteetetaaa gateaaaaca eeeetgtegt eeaeeeteet
                                                                      6.0
cccactccag ggaagctgtg gtcatggtgg tgtggtgaac atcagcaaac cgtctgtggt
                                                                      120
tcagctcaac tggagagggt tttcttatct atatggtgct tgggggtaggg attactctcc
                                                                      180
ccagcatcca aacaaaggac tgtattgggt ggcgccattg aatacagatg ggaaactgtt
                                                                      240
ggagtattat aaactggtac aacacactgg atgatttgct attgtatata aatgctcgag
                                                                      300
aattgeggat cacctatgga ceteggeege gaccaegetg
                                                                      340
      <210> 61
      <211> 179
      <212> DNA
      <213> Homo sapien
     <220>
      <221> misc_feature
      <222> (1)...(179)
      <223> n = A,T,C or G
      <400> 61
tttttgtgac ggacgnttgg agtacatgtc ccaggatcac atccagcagc tagagtggct
                                                                      60
gggacaaget ggeggnggee aageaetgtt gaaacnatag gggtetgggn gnaetegggt
                                                                     120
tnaagtggtt ggtccgantn ttnataacct tgtcngaacc nancatctcg gttgncang
                                                                     179
      <210> 62
      <211> 78
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(78)
      <223> n = A, T, C or G
      <400> 62
agggcgttcg taacgggaat gccgaagcgt gggaaaaagg gagcggtggc nggaagacgg
                                                                      60
ggatgagctt angacaga
                                                                      78
```

```
<210> 63
      <211> 410
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(410)
      \langle 223 \rangle n = A,T,C or G
      <400> 63
cccagttact tggggaggct gaggcaggga gaatcctttg aacccggngg gtgggaggtt
                                                                     60
gcagtgagcc cgagatagca ccattgcact tccancatgg ggtggacaga gtgagactct
                                                                     120
180
tntcccattt caagtcctga aaatagagga tcagaaatgt tgaggaattc tttaggatag
                                                                    240
aaagggagat gggattttac ttatggggaa agaccgcaaa taaagactgn aacttaacca
                                                                    300
cattccccaa gtgnaaggtg ttacccaaga agtaggaacc cttttggctn ttaccttacc
                                                                    360
ttccngaaaa aaacttattn cttaaaatgg aaacccttaa agcccgggca
                                                                    410
      <210> 64
      <211> 199
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(199)
      <223> n = A,T,C or G
      <400> 64
cttgttctca aaaaggtcaa agggagcccg acgaggaata aatagcaatg ccctgaattc
                                                                     60
caactgacct tetacagaaa agtgettgae tgecaagtgg tetteecagt cattagtgag
                                                                    120
gctcttgtag aattctccat actcctcttg ggngangnca tnagggtttn nggcccaaat
                                                                    180
aggntgggcc tngttaagt
                                                                    199
      <210> 65
      <211> 125
      <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(125)
     <223> n = A, T, C or G
     <400> 65
ageggtacag ttetgteetg geateateat teattgtagt atggteaata ggtgeeatga
                                                                     60
aactcagtag cttgctaagg acatgaaacc gaagtttcct gcctttgctg gcctngtngn
                                                                    120
gggta
                                                                    125
     <210> 66
     <211> 204
     <212> DNA
     <213> Homo sapien
```

```
<400> 66
      attcagaatt ctggcatcgg tatttctata aagtccatca gttagagcag gagcaggccc
                                                                             60
      ggagggacgc cctgaagcag cgggcggaac agagcatctc tgaagagccc ggctgggagg
                                                                            120
      aggaggaaga ggagctcatg ggcatttcac ccatatctcc aaaagaggca aaggttcctg
                                                                            180
      tggacctcgg ccgcgaccac gcta
                                                                            204
            <210> 67
            <211> 383
            <212> DNA
            <213> Homo sapien
            <220>
            <221> misc feature
            <222> (1)...(383)
<400> 67
     tcagggcctc caggcagcca gttttgcagg anattcagca cctagngtct tcctgcctna
                                                                            60
     cgctcccaag aacctgctcc tgcaggggga acatcagaac tcgtccttga tgtcaaaatg
                                                                           120
     gggctggtct tnaggcttga agtccaggtt agggctgcca tcctcattga gaattctccg
                                                                           180
     ggcagtgtan ccgacgatgg ggtatttggc tttgtacact ttggtgaaaa cctnatccag
                                                                           240
     ggcctccagt tccttggccg tganacccgt antgtcatgg gtgaggtctg caggatccaa
                                                                           300
     ggacatettg getacecete tagtggagte etteceegte aaggeattgt aaggggetee
                                                                           360
     tcgtccataa aactcctttt cgg
                                                                           383
           <210> 68
           <211> 99
           <212> DNA
           <213> Homo sapien
           <400> 68
     tcacatctcc ttttttttt aactttttca aatttttgtg ttaaatagaa ggctaaaggg
                                                                            60
     ttagatttaa gtttctgcta cattgaccct atttaccta
                                                                            99
           <210> 69
           <211> 37
           <212> DNA
           <213> Homo sapien
           <220>
           <221> misc_feature
           <222> (1)...(37)
           <223> n = A, T, C \text{ or } G
           <400> 69
     gagaaggacn tacggncctg ntantanang aatctcc
                                                                           37
           <210> 70
           <211> 222
           <212> DNA
           <213> Homo sapien
           <220>
           <221> misc_feature
           <222> (1)...(222)
```

```
<223> n = A,T,C or G
      <400> 70
gtgggtcatt tttgctgtca ccagcaacgt tgccacgacg aacatccttq acaqacacat
                                                                          60
tcttgacatt gaagcccaca ttgtccccag gaagagcttc actcaaaqct tcatqqcqca
                                                                          120
tttcgacaga ttttacttcc gttgtaacgt tgactggagc aaaggtgacc accataccqq
                                                                          180
gtttgagaac acccantcac ctgccccggg cggccgctcg aa
                                                                          222
      <210> 71
      <211> 428
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (428)
      \langle 223 \rangle n = A,T,C or G
      <400> 71
caggagtatt ttgtagaaaa gccagaagag cattagtaga tgtatggaaa tatacggtag
                                                                          60
ggcacacgct gacagtactt ttcccaagcc acgccgtatt tcttcttaca gtggtactcq
                                                                         120
tcacgagctt ctcggtggac aagcaacatg gtgaaataaa ttatgtagaa ataaggcaga
                                                                         180
atgtggttaa aaccacatgg gagggaccac gccaaggcca tgatgagatc acccaagtaa
                                                                         240
ttggggtggc gaacaaagcc ccaccatcca gaaactagaa naatttttcc cgttgaaata
                                                                         300
tgaatggntt ttaaatgtgc aagctttgga tcactgggaa ttttcccgaa tgccttttc
                                                                         360
tganaattgc accttnggaa gantccttac cccaagnttc agaccattat ttnaaaaqcn
                                                                         420
ttggaact
                                                                         428
      <210> 72
      <211> 264
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(264)
      \langle 223 \rangle n = A,T,C or G
      <400> 72
gaataaagag cttactggaa tccagcaggg ttttctgccc aaggatttgc aagctgaagc
                                                                          60
tctctgcaaa cttgatagga gagtaaaaag ccacaataga gcagtttatg aagatcttgg
                                                                         120
aggagattga cacacttgat cctgccagaa aatttcaaag acagtagatt gaaaaggaaa
                                                                         180
ggctttggta aaaaaaggtt caggcattcc tagccgantg tgacacagtg gagcanaaca
                                                                         240
tctgcangag actgancggc tgca
                                                                         264
      <210> 73
      <211> 442
      <212> DNA
      <213> Homo sapien ·
                                                                    with the one
      <220>
      <221> misc feature
      <222> (1)...(442)
      \langle 223 \rangle n = A,T,C or G
```

```
<400> 73
ggcgaatccg gcgggtatca gagccatcag aaccgccacc atgacggtgg gcaagaqcaq
                                                                         60
caagatgctg cagcatattg attacaggat gaggtgcatc ctgcaggacg gccggatctt
                                                                        120
cattggcacc ttcaaggctt ttgacaagca catgaatttg atcctctgtg actgtgatga
                                                                        180
gttcagaaag atcaagccaa agaacttcaa acaagcagaa agggaagaga agcgagtcct
                                                                        240
cggtctggng ctgctgccaa gggagaatct ggtctcaatg acngtagaag gaccttcttc
                                                                        300
caaagatact ggnattgctc gagttccact tgctggaact tcccggggcc caaggatcgc
                                                                        360
aaggettetg geaaaagaaa teeanaettn ggeegggaee aeetaaneea atteacaeae
                                                                        420
tggcggccgt actagtggat cc
                                                                        442
      <210> 74
      <211> 337
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(337)
      \langle 223 \rangle n = A,T,C or G
      <400> 74
ggtagcagcg tetecagage etgatetggg gteccagata eccaggeage ageageeetg
                                                                        60
gaggtaaagg gcaagctccc caatgtgagg ggagacccca ttcctggtca gccaggcttt
                                                                        120
cagaggagat agcaggtcga gggagccaac gaagaagaga ctgccancag gggaaggact
                                                                       180
gtcccgccaa ggacagaact gattcagggg ggtcaatgct cctctagaga agagccacac
                                                                       240
agaactgggg ggtccaggaa ccatgaanct tggctgtggt ctaaggagcc aggaatctgg
                                                                       300
acagtgttct gggtcatacc aggattctgg aattgta
                                                                       337
      <210> 75
      <211> 588
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(588)
      <223> n = A,T,C or G
      <400> 75
catgatgagt tetgagetae ggaggaacce teattteete aaaagtaatt tatttttaca
                                                                        60
gcttctggtt tcacatgaaa ttgtttgcgc tactgagact gttactacaa actttttaag
                                                                       120
acatgaaaag gcgtaatgaa aaccatcccg tccccattcc tcctcctct tgagggactg
                                                                       180
gagggaagcc gtgcttctga ggaacaactc taattagtac acttgtgttt gtagatttac
                                                                       240
actttgtatt atgtattaac atggcgtgtt tatttttgta tttttctctg gttgggagta
                                                                       300
tgatatgaag gatcaagatc ctcaactcac acatgtagac aaacattagc tctttactct
                                                                       360
ttctcaaccc cttttatgat tttaataatt ctcacttaac taattttgta agcctgagat
                                                                       420
caataagaaa tgttcaggag agangaaaga aaaaaaatat atgttcccca tttatattta
                                                                       480
gagagagacc cttantcttg cctgcaaaaa gtccaccttt catagtagta ngggccacat
                                                                       540
attacattca gttgctatag gncagcactg aactgcatta cctgggca
                                                                       588
      <210> 76
      <211> 196
      <212> DNA
```

<213> Homo sapien



<400> 76

```
geggtateae ageetggeee eeatgtaeta teggggggee eaggetgeea tegtggteta
                                                                         60
tgacatcacc aacacagata catttgcacg ggccaagaac tgggtgaagg agctacagag
                                                                        120
gcaggccagc cccaacatcg tcattgcact cgcgggtaac aaggcagacc tggacctgcc
                                                                        180
cgggcggccg ctcgaa
                                                                        196
      <210> 77
      <211> 458
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(458)
      \langle 223 \rangle n = A,T,C or G .
      <400> 77
agtagagatg gggtttcact gtgttaacca ggatggtctt gatctcctgg cctcgtgatc
                                                                         60
tgcccgcctc ggcctcccaa agtgttggga ttacaggcgt gaaccaccgc acccqqccaq
                                                                        120
adatgttagt ttttccctat tctctctct ttttcctatt atatacttgg tcaaccagac
                                                                        180
agccatccta ccccanaatg gtaatgcctc ttcattcctc atatgaggga ataaaaqaqa
                                                                        240
aaaaagcttt tggaaaacat ccacttatct aatcatccca aatatgtaat caaaagtata
                                                                        300
caactcatgt gaagaataca ctggtaaaat gttantatag gccaaggtat cttgaattcc
                                                                       360
tatatagaaa gctggtaaat gcccttttgg ctggaaccgc catcttccnn taattcnccc
                                                                       420
aaaatgacca aacacaaagg gnaagangan aagccccc
                                                                       458
      <210> 78
      <211> 464
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(464)
      <223> n = A,T,C or G
      <400> 78
tccgcaaatt tcctgccggc aaggtcccag catttgaggg tgatgatgga ttctgtgtgt
                                                                        60
ttgagagcaa cgccattgcc tactatgtga gcaatgagga gctgcgggga agtactccag
                                                                       120
aggcagcagc ccaggtggtg cagtgggtga gctttgctga ttccgatata gtgcccccag
                                                                       180
ccagtacctg ggtgttcccc accttgggca tcatgcacca caacaaacag gccactgaga
                                                                       240
atgcaaagga ggaagtgagg cgaattctgg ggctgctgga tgcttacttg aagacgagga
                                                                       300
cttttctggt gggcgaacga gtgacattgg ctgacatcac agttgtctgc accctgttqt
                                                                       360
ggctctataa gcaggntcta gaaccttctt ttcgcangac cttcggccgg accacgctta
                                                                       420
acccaaattc cacacattg cnggccgtac taanggaatc ccac
                                                                       464
      <210> 79
      <211> 380
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(380)
      <223> n = A,T,C or G
```



```
<400> 79
 ctgtatgacc agtttttcca tctccttcac ttctaccttg atcagctcga agtccagttc
                                                                          60
 agtgtaagaa atggtatcct tctccatgat gtcaattcgg acagttaggt ttaacagttt
                                                                         120
 cttttcatac acactaatta attggacata ttccctcact ttanaaagtt ctttctcaaa
                                                                         180
 cttctganaa aagaacatga actgtgaatt ccaagcgttc ccactctgtc cacgggaaaa
                                                                         240
 ggtggtgtct ggcagggaaa cagaacactg gcaggtccac ggtcatccac ggagccggtg
                                                                         300
  aaattgggaa aacaactggg acacagaacc tccgctgcct aagctgcggn tgggagcttg
                                                                         360
 gaacccgacc tggaactgga
                                                                         380
        <210> 80
        <211> 360
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc feature
        <222> (1)...(360)
        <223> n = A, T, C or G
        <400> 80
 tegageggee geeegggeag gteeteagag agetgtttgt tnegettett caaaaactee
                                                                          60
 tattctccac ttctgctaaa ggactggatg acatcaattg tgatagcaat atttgtgggt
                                                                         120
 gttctgtcan ncancatcgc actcctgaac aaagtagatg ttggattgga tcagtcttt
                                                                         180
 tccacccaga tgactcctan atggtggatn atttcaaatc catcantcag tacctgcatg
                                                                         240
 cgnggtccgc ctgtgtnctt tgtcctgcag gangggcnct actacacttc ttccnagggg
                                                                         300
 canaacatgg tgtgcngcgg ccatgggctg gcaacantga ttcnctgctg cacccanatn
                                                                         360
        <210> 81
        <211> 440
       <212> DNA
        <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(440)
       <223> n = A, T, C \text{ or } G
       <400> 81
 acgtggtccg gcgagtctga cctgcagata tgaactcctt gggaaaccta cattctgcct
                                                                          60
 cagacatact gggggcaaat ggctttaaaa gtctggctca gggagccaag attacagaaa
                                                                         120
nccgttgagt cnccatacat ggacactgac aaaggaactg aagatatcca aacaagccct
                                                                         180
 cctggtcccg ngcctgcata aagatcggga ncggaacggt accngacgtc tgtggtcagg
                                                                         240
 ggttgtggaa aattggaaaa aaccagtcct gcccacattg acagggaagc ctcaacggaa
                                                                         300
 attgaacaga tngtcttatc accagtctcc cctcctggat cntgtctcgg ctcnggggan
                                                                         360
 tcagtgatca gtcctttcag gtggaagaag caaagaagat caacaanaag cngatcctct
                                                                         420
 cacctgntac cagcatatgg
                                                                         440
       <210> 82
       <211> 264
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
```

```
<222> (1)...(264)
      <223> n = A,T,C or G
      <400> 82
agcgtggtcg cggccgangt cctgacattc ctgccttctt atattaatta tacnaataaa
                                                                         60
acaaaatagt gttgaagtgt tggagcggcg aaaatttttg gggggtggta tggacagaga
                                                                        120
atqqqcqatn ttctcanggc tgcttcaagt gggattgggg cngcgtggga tcatncagtg
                                                                        180
gganagattn cnctgaccgg antctnttgg tanggatnat cttgtgggga tgtgcaagag
                                                                        240
ncattcgtct cctgaatgan tggt
                                                                        264
      <210> 83
      <211> 410
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(410)
      <223> n = A, T, C \text{ or } G
      <400> 83
                                                                         60
ancytygtcy cygccyanyt ccacayttyt gygagaycca yccattytyy gygcayctco
                                                                        120
acaggtaaga ctcgtgtcct gagcagcgca catcatccag gacaatgggt cctgagccct
qaccaaaccg ggcatttcct ggggctgaca tggcccagcc acagcccant tgcctgcaga
                                                                        180
cgaaattggc atcattggtg tcccagtant catcacacac ggtgccccag gaacctccgg
                                                                        240
tatangaact ccacteggee tenanacetg tegeeteeat teencageet cagggggeaa
                                                                        300
                                                                        360
actgggattc agatectict gigggtacag giggtgatat cetgacagge caactiteig
                                                                        410
gcctgagtgt tgactgangc tgggcagacc tgcccgggcg gccgctcgaa
      <210> 84
      <211> 320
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(320)
      <223> n = A,T,C \text{ or } G
      <400> 84
tègaacggcc gcccgggcag gtctgcccca ggtgtatcca tttgccgccg atctctatca
                                                                         60
naaggagetg getaeeetge nnegaegaan teetgaanat aateteaeee neeeagatet
                                                                        120
ctctgtcgca atggagatgt cgtcatcggt ggncctgatc acagggcatt ggactcagag
                                                                        180
anangtnanc acagtgtnga agcgattgan nnagttcagt tgctggtctt acccgatntt
                                                                        240
qqaaqqaaqq aaaacqtqtt angacqtatc tcgatgnant tgaccaaanc tgaanqctnc
                                                                        300
                                                                        320
agggggcatc gcaaaganan
      <210> 85
      <211> 218 · · ·
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (218)
```

```
<223> n = A,T,C or G
        <400> 85
 tegageggee geeegggeag gtetgetgee egtgetggtg ceattgeeee atgtgaagte
                                                                           60
 actgtgccag cccagaacac tggtctcggg cccgagaaga ctcctttctc caggctntan
                                                                          120
 gtatcaccac taaaatctcc aggggcacca tnganatcct gggtgtccgc aatgttgcca
                                                                         180
 atgtctgtcc gcnnattggc tacccaactg ttgcatca
                                                                         218
        <210> 86
        <211> 283
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc feature
        <222> (1)...(283)
       \langle 223 \rangle n = A,T,C or G
       <400> 86
 tcgacttctt gtgaaggttt tgganaaata tgtatcagtt cgttttattt gggtattcaa
 taatateett ggtgataatg etgaeteeat ggettetgae eccaaaaatt gaeeetgetg
                                                                          60
                                                                         120
 ccactggttg tagccctgag attgattttt gtagccacga ttgtttcctc gtcctctgaa
                                                                         180
 gtnctggttg tanttccctc tgtngggcat tcccctctgt tgtanttccc tctgtttgan
                                                                         240
 taactaccac ggccaggaaa aacaggggca cgaaggtatg gat
                                                                         283
       <210> 87
       <211> 179
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(179)
       <223> n = A,T,C or G
       <400> 87
agcgtggtcc cggccgatgt ctttctgtgt aagtgcataa cactccacat acttgacatc
                                                                         60
cttcangtca cgggccagct nttcagcant ctctggagtg ataggctact gtntgttctn
                                                                        120
ggcaagtgtc tcaanaatac aggggtcntc tctgagatga ntttcagtcc cgaaccctc
                                                                        179
       <210> 88
       <211> 512
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(512)
      <223> n = A,T,C or G
      <400> 88
tcgagcggcc gcccgggcag gtcctancan agaatcacca aatttatgga gagttaacag
                                                                        60
gggtttaaca ggaangaagt gcctttagta agttctcaag ccagangctg gaggcagcag
                                                                        120
ctaaatcaga ggacaggatc ctcagtgaaa gtgagccatt cggggtggca tgtcactcca
                                                                        180
ggaataagca caacttanaa acaaatgatt tcgtangata gcacagtgac attggtgcac
                                                                        240
```

```
ttgtgaacct gaggccactg tgtcaaactg tgcactggtt gtgaataggg aganccaaaa
                                                                         300
attatgtcct actgggtaat gagctttcaa tgggctcgat cctctcacnc tgaaagctct
                                                                         360
gtagagcagc tcagaaccac aaccactccc aacattgacc cttctggggg tactgtctgt
                                                                         420
ggcacccaca ggaaggagct ggagatcccc attaggactg tccacccaca cttgaagcca
                                                                         480
caaaactgca cctcggccgc gaccaccgct ta
                                                                         512
      <210> 89
      <211> 358
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(358)
      \langle 223 \rangle n = A,T,C or G
      <400> 89
tegageggge egeeegggea ggtetgeeag teeceateee agacattett tgeatetaag
                                                                         60
ctgangtctg aactgagtgg ggtgggctgg tgtttccatc ctcacaactc cagtgagccg
                                                                         120
ggtgtggccg tggcctgcgt ctctctggcg gttagtgatg ttggcatcat ccaccttttt
                                                                        180
caaaacaaaa gcactggact gaagaanaat cccnccctgt ntccacccag tccatggttt
                                                                        240
ttaataaaag ggttatnnaa gttgancaag ncatcaccac acacaancct aagaacnttt
                                                                        300
ttcatcnntc cccaaaacaa accencaccc tgggaactcc gggcgcgaac cacgccta
                                                                        358
      <210> 90
      <211> 250
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(250)
      <223> n = A, T, C \text{ or } G
      <400> 90
cgagcggccg cccgggcagg tctggatggg gagacggact ggaactgcgg cttcccgtgg
                                                                         60
cctgcacgca caaggctccc cacggccgcc gaccttcttc agattcgatc gtatgtqtac
                                                                        120
gcacnaagag ccaaatattg acattcacaa cttcgtggga atnttacccc anaagactgc
                                                                        180
gaccccccga tcaggcgana gcctgagcat agaagaacac cgctgtgggc ttggcactgt
                                                                        240
gggncccatc
                                                                        250
      <210> 91
      <211> 133
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(133)
      <223> n = A, T, C \text{ or } G
      <400> 91
tcgagcggcc gnccgggcag gtcccgggtg gttgtttgcc gaaatgggca agttcntnaa
                                                                         60
ncctgggaag gtggtgcntg tnctggctgg acgctactcc ggacgcnaag ctgtcntcgt
                                                                        120
gangancatt gat
                                                                        133
```

420

```
<210> 92
       <211> 232
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(232)
       <223> n = A,T,C or G
       <400> 92
 agcgtggtcg cggccgangt ctgtcacttt gcgggggtag cggtcaattc cagccaccag
                                                                          60
 agcatggctg taggggcgat ctgaggtgcc atcatcaatg ttcttcacga tgacaagctt
                                                                         120
 tgcgteegga.gtagegteea.geeaggaraa geaceacett cecaegtnit cangaactng
                                                                         180
 cccatttcgg cataaccacc cgggacctgc ccgggcggnc gctcgaaaag cc
                                                                         232
       <210> 93
       <211> 480
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(480)
       <223> n = A,T,C or G
       <400> 93
agegtgggte geggeegang tetgtanget caceggeeag agaagaceae tgtgageatt
                                                                         60
ttgccgtata tcctgccctg ccatttgttc actttttaaa ctaaaatagg aacatccgac
                                                                        120
acacacegtt tgcategtet tetecettga tattttaage atttteceat gtegtgagtt
                                                                        180
tctcagaaac atgtttttaa caattgtact atttagtcat ngtccattta ctataattta
                                                                        240
tctgaccatt tccctactgt taaaatactt aagacggttt ctgatttttc cactatttaa
                                                                        300
ataatgctgt gatgaatatc tttaaaatct tctgatttct tacttttttc ccccttagat
                                                                        360
gcctggaagt ggtattttga ggtgaaagag tttgttcatt ttgaanatat ttctgtctct
                                                                        420
ctctcgacct gatgtgtana cgctcacttc cagttagcag aaccacctta gtttgtgtct
                                                                        480
      <210> 94
      <211> 472
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(472)
      <223> n = A, T, C or G
      <400> 94
tegageggne geeegggeag ggtetgatgt canteacaae ttgaagggat geeaatgatg
                                                                        60
taccaatcon atgtgaaatc totoototta totootatgo tgganaaggg attacaaagt
                                                                       120
tatgtggcng ataannaatt ccatgcacct ctantcatcg atgagaatgg agttcatgan
                                                                       180
ctggtgaacn atggtatctg aacccgatac cangttttgt ttgccacgat angantagct
                                                                       240
tttatttttg atagaccaac tgtgaaccta ccacacgtct tggacnactg anntctaact
                                                                       300
atconcaggg ttttattttg cttgttgaac tcttncagct nttgcaaact tcccaagatc
                                                                       360
canatgactg antitcagat agcatttta tgattcccan ctcattgaag gtcttatnta
```

```
tntcnttttt tccaagccaa ggagaccatt ggacctcggc cgcgaccacc tn
                                                                        472
      <210> 95
      <211> 309
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(309)
      \langle 223 \rangle n = A,T,C or G
      <400> 95
tcgagcggcc gcccgggcag agtgtcgagc cagcgtcgcc gcgatggtgt tgttggagag
                                                                         60
cgagcagttc ctgacggaac tgaccagact tttccanaag tgccggacgt cgggcancgt
                                                                        120
ctatatcacc ttgaagaant atgacggtcg aaccaaaccc attccaaaga aangtactgt
                                                                        180
gganggettt ganceegeag acaacnagtg tetgttaaga actacegatn ggaaanaana
                                                                        240
anatcagcac tgtgggtgag ctccnaggga agttaataan tttcggatgg gcttattcna
                                                                        300
acctcctta
                                                                        309
      <210> 96
      <211> 371
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(371)
      <223> n = A.T.C or G
      <400> 96
tcgagcggcc gcccgggcag gtccaccact cacctactcc ccgtctctat agatttgcct
                                                                        60
gttctgggca gttctcagca atggaatcct actgtgtatc tttttgtgac tggttcttta
                                                                       120
actcagcatc acattttcaa ggttcatcca tgctgcagcc tggctccgta ctggtgacag
                                                                       180
tacttcattt ctctcccct tttgttcaga ccaaggtctc cctctgtccc caaggctaaa
                                                                       240
gtgcagttgg tgtgatcatg gctcactgca gcctcaaact cctggactca aacagtcctc
                                                                       300
ccatctcage eteccaaagt getgatntta taagttgcaa geeetgcace cageetgtat
                                                                       360
ctccagtttg t
                                                                       371
      <210> 97
      <211> 430
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(430)
      <223> n = A,T,C or G
      <400> 97
tcgancggcc gcccgggcag gtttnttttn tttnttttt nnnngntagt atttaaagan
                                                                        60
atttattaaa tcatcttatc accaaaatgg aaacatnttc caactagaaa catgcnacca
                                                                       120
tcatcttccc cagtccagtc ncaangtcca atattttnct tgcctctgca gataaaaagt
                                                                       180
tennattttt atacceacte ttacteccee ceaaaatttt aattengtee tneectaaaa
                                                                       240
ttncnccggg taacaantta ccaaaatggc naaccaatta ttttaaanaa aagttgcncn
                                                                       300
```

```
ttnaaaangg aaactttntg gcaanttanc ctcttttccc ttcccacccc ccantttaag
  gggaaaacaa tggcactttg ctcttgcttn aacccaaaat tgtcttccaa aaactattaa
                                                                          360
                                                                         420
  aaatgttnaa
                                                                         430
        <210> 98
        <211> 307
        <212> DNA
        <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(307)
       <223> n = A, T, C or G
 tenaacggee geeenggenn gtetngenge acetgtgeet cancegtega tacetggteg
 attgggacan ggaanacaat ntggttttca gggaggccac anatttggag aaacggatga
                                                                          60
 atteteettt atteegaant cageteettg gteteegtag anggtgatet tgaaattete
                                                                         120
 ctgttttgaa aactttcttg aanaaacctt acctgctggt tgtatttggt ctcccactcg
                                                                         180
 gacaagtact cgttatccnn ggtactctta atgtgcccac gtnaactccc cgggntggca
                                                                         240
                                                                        300
 actggaa
                                                                        307
       <210> 99
       <211> 207
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(207)
       <223> n = A,T,C or G
       <400> 99
gtccnggacc gatgttgcna aganntttct tggtccanta ggttcnaaaa aatgataanc
naggtntanc acgtgaagat ntntatanag tcttantnaa aacncntaga tctgnatgac
                                                                         60
gataantcga anacnggggg aggggntgag gngaggtggn gtganggaag anntgttgat
                                                                        120
                                                                        180
aaaagannna gntgataaga anngagc
                                                                        207
      <210> 100
      <211> 200
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(200)
      <223> n = A,T,C or G
      <400> 100
acntnnacta gaantaacag ncnttctang aacactacca tctgtnttca catgaaatgc
cacacacata naaactccaa catcaatttc attgcacaga ctgactgtaa ttaattttgt
                                                                        60
cacaggaatc tatggactga atctaatgcn nccccaaatg ttgttngttt gcaatntcaa
                                                                       120
                                                                       180
acatnnttat tccancagat
                                                                       200
      <210> 101
```

```
<211> 51
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(51)
      <223> n = A,T,C or G
      <400> 101
tcgagcggcc gcccgggcag gtctgaccag tgganaaatg cccagttatt g
                                                                        51
      <210> 102
      <211> 385
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(385)
      <223> n = A,T,C or G
      <400> 102
aacgtggtcg cggccgaagt ccatggtgct gggattaatc cactgtgacn gtgactctga
                                                                        60
gttgagttgt ttttcaatct tctccaagcc tgtggactca tcctccacat ccttgggtag
                                                                       120
taggatgaac atgctgaaga tgctnatttt gaaaaggaac tctatgaatc ttacaattga
                                                                       180
atactgtcaa tgtttcccca tnacagaacg tggnccccca aggttccatc atctgcactg
                                                                       240
ggtttgggtg ttctgtcttg gttgactctt gaaaagggac atttctttt gttttcttga
                                                                       300
attcanggaa attttcttca tccactttgc ccacaaaagt taggcagcat ttaaccccca
                                                                       360
anggattttg ggtctgggtc cttcc
                                                                       385
      <210> 103
      <211> 189
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(189)
      <223> n = A, T, C \text{ or } G
      <400> 103
agcgtggtcg cggccgaagt ctgcagcctg ggactgaccg ggaagctctg attatttacc
                                                                       60
caccacaggt angitgigtt cigaatcica agitcacagg tiaaggciac agcatcica
                                                                       120
tcctccacgg ggttggantt gttgctggtg atgaanggtt tggggtggct ctgcataact
                                                                       180
gttgatctc
                                                                       189
      <210> 104
      <211> 181
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(181)
      <223> n = A,T,C or G
```

```
<400> 104
  tcgagcggcc gcccgggcag gtccaggtct ccaccaangc accaccgtgg gaagctggta
                                                                                    60
  attgatgccc accttgaagc cnntggggca ccatccncca actggatgct gcgcttggtt
                                                                                   120
  ttgatggtgg caatggcaca ttgactcttt tgggaaccac ttcaccacgg tacaacaggc
                                                                                   180
                                                                                   181
         <210> 105
         <211> 327
         <212> DNA
         <213> Homo sapien
         <220>
        <221> misc_feature
entronoli, cantotegiano no notamo i monamente infermento canto e fin entelegen consecutare destrutura esta esta
Entronoli, cantotegiano no notamo i monamente infermento canto e fin entelegen consecutare destrutura esta esta
        \langle 223 \rangle n = A,T,C or G
        <400> 105
 tcgagcggcc gcccgggcag gtcttctgtg gagtctgcgt gggcatcgtg ggcagtgggg
                                                                                   60
 ctgccctggc cgatgctcan aaccccagcc tctttgtaaa gattctcatc gtgganatct
                                                                                  120
 ttggcagcgc cattggcctc tttggggtca tcgtcgcaat tcttcanacc tccanaatga
 anatgggtga ctanataata tgtgtgggtn gggccgtgcc tcacttttat ttattgctgg
                                                                                  180
                                                                                  240
 ttttcctggg acagaactcg ggcgcgaaca cgcttanccg aattccaaca cactggcggg
                                                                                  300
 cgttactagt ggatccgagc tcggtac
                                                                                  327
        <210> 106
        <211> 268
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc_feature
        <222> (1)...(268)
        <223> n = A,T,C or G
        <400> 106
 agegtggteg eggeegangt etggegtgtg ceacateggt eccaeetege tttacaaaae
                                                                                  60
agtectgaac tinatetaat aaaattattg tacacnacat tiacattaga aaaaganage
                                                                                 120
tgggtgtang aaaccgggcc tggtgttccc tttaagcgaa ngtggctcca cagttggggc
                                                                                 180
atcgtcgctt cctcnaagca aaaacgccaa tgaaccccna agggggaaaa aggaatgaag
                                                                                 240
 gaactgneen gggangneeg eteegaaa
                                                                                 268
       <210> 107
       <211> 353
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(353)
       \langle 223 \rangle n = A,T,C or G
       <400> 107
tcgagcggcc gcccgggcag gtggccaggc catgttatgg gatctcaacg aaggcaaaca
                                                                                  60
cctttacacn ctagatggtg gggacatcat caacgccctg tgcttcagcc ctaaccgcta
                                                                                120
```

```
ctggctgtgt gctgccgcag gccccagcat caagatctgg gatttanagg gaaagatcnt
                                                                        180
tgtnnatgaa ctgaancnta aattatcagt tccannacca ngcaaaaacc acccngtgca
                                                                        240
ctccctggcc tggtctgctg atgggacctc gggcgcgaac acgctnancc caattccanc
                                                                        300
acactgggcg gncgttacta ntggatccga actcnggtac caancttggc gtt
                                                                        353
      <210> 108
      <211> 360
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(360)
      <223> n = A, T, C \text{ or } G
      <400> 108
agcgtggtcg cggccgaagt cctggcctca catgaccctg ctccagcaac ttgaacagga
                                                                         60
naagcagcag ctacatcctt aaggtccgga aagttagatg aagatttgga tcctgcattg
                                                                        120
nectgeetee caectatete teeenaatta taaacageet eettgggaag cagcagaatt
                                                                        180
taaaaactct cccnctgccc tnttgaacta cacaccnacc gggaaaacct ttttcanaat
                                                                        240
ggcacaaaaa tncnagggaa tgcatttcca tgaangaana aactgggtta cccaaaatta
                                                                        300
ttgggttggg gaaatccngg gggggttttn aaaaaagggc aancenecaa anaaaaaaac
                                                                        360
      <210> 109
      <211> 101
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(101)
      <223> n = A, T, C \text{ or } G
      <400> 109
atogtggton eggeegaagt cetgtgteet ggatgggeeg tgtgcanega ateegttgge
                                                                         60
gactcctaac taccaanaaa angactctcg gaagaaattt c
                                                                        101
      <210> 110
      <211> 300
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(300)
      <223> n = A, T, C \text{ or } G
      <400> 110
ccanggaaac ccagagtcac atgagatagg gtggctttcg ggacaggggg tcagangaat
                                                                         60
ggtacatgga teteageece tgatggacae ggaacaggtg tggteagaae teecangatt
                                                                        120
ctgcatccan gatccagtct ctatagaagt tatggatcat tccttcattt cattccccc
                                                                        180
ttcatgaaaa aacttctgaa caagcctttt ttctcacttt ggggccctgt ttggcncaag
                                                                        240
gtnttnantt ggggaaaaaa aaacaaatcc nttccnttan ccctccgtgg ggaatgacct
                                                                        300
```

<210> 111

```
<211> 366
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(366)
       <223> n = A, T, C or G
       <400> 111
 cgagcggccg cccgggcagg tccttgtgtt gccatctgtt ancattgatt tctggaatgg
                                                                       60
 aacanctttc tcaaagtttg gtcttgctan tcatgaagtc atgtcagtgt cttaagtcac
                                                                      120
 tgctgctcac ttccttaccc agggaatata ctgcataagt ttctgaacac ctgttttcan
                                                                      180
 tattcactgt teeteteetg eccaaaattg gaagggaeet catttaaaaa teaaatttga
                                                                      240
 atcctgaaan aaaaacngga aatntttctc ttggaatttg gaatagaatt attcanttga
                                                                      300
 ataacatgtt ttttcccctt gccttgctct tcncaanaac atctggacct cggccgcgac
                                                                      360
 acctta
                                                                      366
       <210> 112
       <211> 405
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(405)
      <223> n = A, T, C or G
      <400> 112
ctgactncta aacttctaat tcnatcaana taactactct ccttccgtct tncagagtgt
tcacaataaa tctgtgaatc tggcatacac agttgctgga aaattgttct tcctccacna
                                                                      60
                                                                     120
aaaggtcaat tgttcnccnc atgaaanaag ataaattgtt catccatcac tnctgaacca
tccaaaacgc cggcggaatt attnccccgt tattatgggg aacggaattt tnaataaatt
                                                                     180
tgggaangaa tggggctttt attgttttgt tttccccctt tcttggcatt gattgggccg
                                                                     240
                                                                     300
caatgggccc cctcgctcan aanntgcccc ggggccggcc gctccaaaac cgaaattccc
                                                                     360
anccacactt ggcgggccgt tactanttgg atccgaactc ggtta
                                                                     405
      <210> 113
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 113
ggatagaaga gtatatgggt ttggcaccac ggggtggata ggcaaaacat ttggttgata
                                                                     60
aggegeagat tetgaactaa ettgtaagge ttgtetggtt ttaggacagg taaaatgggg
gaatggtaag gagagtttat aggttttagg agcccatgct gtagcaggca agtgataaca
                                                                     120
                                                                     180
ggctttaatc ctttcaaagc atgctgtggg atgagatatt ggcatttgag cggggtaagg
240
tagaggtatc ttatacttgt ggggttaagg tgggggggat ataagaggga ggacgccaaa
                                                                    300
ggaggctttg gattaggaat aaggggcggc aatgagatgc a
                                                                    360
                                                                    401
     <210> 114
     <211> 401
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1)...(401)
      <223> n = A, T, C \text{ or } G
      <400> 114
angtecacag gangeangag gecaggetee gteceancea gtecatgatg ttgaagagga
                                                                          60
ggaagcagca catggggttg aagaactgac tecaetteee aggaetggtg gagetggtea
                                                                         120
ccatggctgt ggtggcgggg aagacggaca gggtgacttc tggaagacag tgaagactga
                                                                         180
aggitticct ggcttctggg gctcatctgg ctctgattcc ggctccttct ccaggicaag
                                                                         240
atccagggtt cagagetact ttettggggg actaetnggg aatcccgtte teatetgggg
                                                                         300
gtngaggggg gacggggnaa gggncatgct tgtgacccag gtttcccacc tcggcccgcg
                                                                         360
accacgctaa ggcccgaatt ncagcacact tggcggcccg t
                                                                         401
      <210> 115
      <211> 401
      <212> DNA
      <213> Homo sapien
      <400> 115
atccctgtaa gtctattaaa tgtaaataat acatacttta caacttctct tagtcggccc
                                                                         60
ttggcagatt aaatctttgc aaaattccat atgtgctatt gaaaaatgaa ataaaacctc
                                                                         120
agatgtctga attcttattt caaatacagt tatataatta ttttaaatta caatatacaa
                                                                        180
tttctgttaa atacaactgt taagggattc tgagaacaat tataagatta taataatata
                                                                        240
tacaaactaa cttctgaaat gacatgggtt gtttccttcc caccctccta ccctctcaaa
                                                                        300
gagtttttgc atttgctgtt cctggttgca aaaggcaaaa gaaaatctaa aaatagtctg
                                                                        360
tgtgtgtcca cgacatgctc gctcctttga gaatctcaaa c
                                                                        401
      <210> 116
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      <223> n = A, T, C \text{ or } G
      <400> 116
ngatttaatt gnnagcttct ttttaatgga atnnttggct aaaatgaatt gatqattatg
                                                                         60
aatateeeta ggaggagtta geatggannn tgateatttt ettngnacte etttangaca
                                                                        120
nggaaacagg natcagcatg anggtancan aaaccttatn accnangcgc acganctgac
                                                                        180
ttcttccaaa gagttgnggt tccgggcagc ggtcattgcc gtgcccattg ctggagggct
                                                                        240
gattctagtg ntgcttatta tgctggccct gaggatgctt ccaanatgaa aataagangc
                                                                        300
t
                                                                        301
      <210> 117
      <211> 383.....
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (383)
```

```
<223> n = A, T, C or G
```

```
<400> 117
  aattgcaact ggacttttat tgggcagtta cnacaacnaa tgttttcana aaaatatttg
                                                                                                                                                    60
  gaaaaaatat accacttcat agctaagtct tacagagaan aggatttgct aataaaactt
                                                                                                                                                  120
  aagttttgaa aattaagatg cnggtanagc ttctgaacta atgcccacag ctccaaggaa
                                                                                                                                                  180
  nacatgtcct atttagttat tcaaatacca gttgagggca ttgtgattaa gcaaacaata
                                                                                                                                                  240
  tatttgttan aactttgntt ttaaattact gntncttgac attacttata aaggagnctc
                                                                                                                                                  300
  taactttcga tttctaaaac tatgtaatac aaaagtatan ntttccccat tttgataaaa
                                                                                                                                                  360
  gggccnanga tactgantag gaa
                                                                                                                                                  383
              <210> 118
              <211> 301
              <212 > DNA
   ~_____________Homo-sapiental and a company of the c
              <400> 118
 ctgctagaat cactgccgct gtgctttcgt ggaaatgaca gttccttgtt ttttttgttt
                                                                                                                                                   60
 ctgtttttgt tttacattag tcattggacc acagccattc aggaactacc ccctgccca
                                                                                                                                                 120
 caaagaaatg aacagttgta gggagaccca gcagcacctt tcctccacac accttcattt
                                                                                                                                                 180
 tgaagttcgg gtttttgtgt taagttaatc tgtacattct gtttgccatt gttacttgta
                                                                                                                                                 240
 ctatacatct gtatatagtg tacggcaaaa gagtattaat ccactatctc tagtgcttga
                                                                                                                                                 300
                                                                                                                                                 301
              <210> 119
              <211> 401
             <212> DNA
             <213> Homo sapien
             <400> 119
 taaggacatg gacccccggc tgattgcatg gaaaggaggg gcagtgttgg cttgtttgga
                                                                                                                                                  60
 tacaacacag gaactgtgga tttatcagcg agagtggcag cgctttggtg tccgcatgtt
                                                                                                                                                 120
 acgagagcgg gctgcgtttg tgtggtgaat ggggaggaaa tgtcactgcc gaagaccaaa
                                                                                                                                                 180
aacaagcttc ttggtataaa agactcttac agaatatgtg tattgtaatt tattgatctg
                                                                                                                                                240
gatgcttaag tgtcatggac agtaaatgaa tttgaacttt atgtttgagg acatgacatt
                                                                                                                                                300
gggtttgaaa atataaactg cttttgagca gtttaagtca gggcatttga gaataaaata
                                                                                                                                                360
ggaactttct cttcagtttg taaaactctc ttgccctctc t
                                                                                                                                                401
             <210> 120
             <211> 301
             <212> DNA
             <213> Homo sapien
             <400> 120
tccagagata ccacagtcaa acctggagcc aaaaaggaca caaaggactc tcgacccaaa
                                                                                                                                                 60
ctgccccaga ccctctccag aggttggggt gaccaactca tctggactca gacatatgaa
                                                                                                                                                120
gaagetetat ataaateeaa gacaageaae aaaceettga tgattattea teaettgggt
                                                                                                                                                180
gagtgcccac acagtcaagc tttaaagaaa gtgtttgctg aaaataaaga aatccagaaa
                                                                                                                                               240
ttggcagage agtttgtcct cetcaatetg gtttatgaaa caactgacaa acacetttet 3 300
C
                                                                                                                                               301
            <210> 121
            <211> 2691
            <212> DNA
            <213> Homo sapien
```

<400> 121 gettgeeegt eggtegetag etegeteggt gegegtegte eegeteeatg gegetetteg 60 tgcggctgct ggctctcgcc ctggctctgg ccctgggccc cgccgcgacc ctggcgggtc 120 ccgccaagtc gccctaccag ctggtgctgc agcacagcag gctccggggc cgccagcacg 180 gccccaacgt gtgtgctgtg cagaaggtta ttggcactaa taggaagtac ttcaccaact 240 gcaagcagtg gtaccaaagg aaaatctgtg gcaaatcaac agtcatcagc tacgagtgct 300 gtcctggata tgaaaaggtc cctggggaga agggctgtcc agcagcccta ccactctcaa 360 acctttacga gaccetggga gtcgttggat ccaccaccac tcagetgtac acggaccgca 420 cggagaaget gaggeetgag atggaggge ceggeagett caccatette geeectagea 480 acgaggeetg ggeeteettg eeagetgaag tgetggaete eetggteage aatgteaaca 540 ttgagetget caatgeeete egetaceata tggtgggeag gegagteetg actgatgage 600 tgaaacacgg catgaccete acctetatgt accagaatte caacatecag atccaccact 660 atectaatgg gattgtaact gtgaactgtg ceeggeteet gaaageegae caccatgeaa 720 ccaacggggt ggtgcacctc atcgataagg tcatctccac catcaccaac aacatccagc 780 agatcattga gatcgaggac acctttgaga cccttcgggc tgctqtqqct qcatcaqqqc 840 tcaacacgat gcttgaaggt aacggccagt acacgctttt ggccccgacc aatgaggcct 900 togagaagat coctagtgag actitgaaco gtatootggg cgacccagaa gccctgagag 960 acctgctgaa caaccacato ttgaagtcag ctatgtgtgc tgaagccato gttgcqqqqc 1020 tgtctgtaga gaccetggag ggcacgacac tggaggtggg ctgcagcggg gacatgctca 1080 ctatcaacgg gaaggcgatc atctccaata aagacatcct agccaccaac ggggtgatcc 1140 actacattga tgagctactc atcccagact cagccaagac actatttgaa ttggctgcag 1200 agtotgatgt gtocacagoo attgacottt toagacaago oggootoggo aatoatotot 1260 ctggaagtga gcggttgacc ctcctggctc ccctgaattc tgtattcaaa qatqqaaccc 1320 ctccaattga tgcccataca aggaatttgc ttcggaacca cataattaaa gaccagctgg 1380 cctctaagta tctgtaccat ggacagaccc tggaaactct gggcggcaaa aaactgagag 1440 tttttgttta tcgtaatagc ctctgcattg agaacagctg catcgcggcc cacgacaaga 1500 gggggaggta cgggaccctg ttcacgatgg accgggtgct gacccccca atggggactg 1560 tcatggatgt cctgaaggga gacaatcgct ttagcatgct ggtagctgcc atccagtctg 1620 caggactgac ggagaccctc aaccgggaag gagtctacac agtctttgct cccacaaatg 1680 aagcetteeg ageeetgeea eeaagagaac ggageagaet ettgggagat geeaaggaac 1740 ttgccaacat cctgaaatac cacattggtg atgaaatcct ggttagcgga ggcatcgggg 1800 ccctggtgcg gctaaagtct ctccaaggtg acaagctgga agtcagcttg aaaaacaatg 1860 tggtgagtgt caacaaggag cctgttgccg agcctgacat catggccaca aatggcgtgg 1920 tccatgtcat caccaatgtt ctgcagcctc cagccaacag acctcaggaa agaggggatg 1980 aacttgcaga ctctgcgctt gagatcttca aacaagcatc agcgttttcc agggcttccc 2040 agaggtctgt gcgactagcc cctgtctatc aaaagttatt agagaggatg aagcattagc 2100 ttgaagcact acaggaggaa tgcaccacgg cagctctccg ccaatttctc tcagatttcc 2160 acagagactg tttgaatgtt ttcaaaacca agtatcacac tttaatgtac atgggccgca 2220 ccataatgag atgtgagcct tgtgcatgtg ggggaggagg gagagagatg tactttttaa 2280 atcatgttcc ccctaaacat ggctgttaac ccactgcatg cagaaacttg gatgtcactg 2340 cctgacattc acttccagag aggacctatc ccaaatgtgg aattgactgc ctatgccaag 2400 tccctggaaa aggagcttca gtattgtggg gctcataaaa catgaatcaa gcaatccagc 2460 ctcatgggaa gtcctggcac agtttttgta aagcccttgc acagctggag aaatggcatc 2520 attataagct atgagttgaa atgttctgtc aaatgtgtct cacatctaca cgtggcttgg 2580 aggettttat ggggeeetgt eeaggtagaa aagaaatggt atgtagaget tagattteee 2640 tattgtgaca gagccatggt gtgtttgtaa taataaaacc aaagaaacat a 2691

<210> 122

<211> 683

<212> PRT

<213> Homo sapien

<400> 122

Met Ala Leu Phe Val Arg Leu Leu Ala Leu Ala Leu Ala Leu

1				5					10					1 =	
Gl	y Pro	o Al	a Al		r Lei	ı Ala	a Gly	y Pro	o Al	a Lv	s Se:	r Pro	o Tv	15 r Gli	n Leu
			20					25					3.0		
		35					40					45			n Val
	50					55					60				Asn
65					70					75					l Ile 80
				85					90					95	Gly
			100)				105	5				110	ı Gly	v Val
Val	. Gly	ser ser	Thi	Thr	Thr	Gln	Leu	Tyr	Thr	Asp	Arg	Thr	Glu	Lvs	Leu
Arc	Pro	GJ1	Met	- Gli	Gla	Dro	-1-2-0	Marine Comment	r Parage of	magaring: 1-ab (i	electricis representativo	1-2/5	Control of white	· - va mais in district	-
	130	,				135					140)			Ser
145	. 610	AIC	ıırp) Ala	150	Leu	Pro	Ala	Glu	Val 155		Asp	Ser	Leu	Val
Ser	Asn	Val	Asn	Ile			Leu	Asņ	Ala	Leu	Arq	Tvr	His	Met	160 Val
				165)				170					175	
			T80					185					190		Thr
		132					200					205	Pro	Asn	Gly
Ile	Val 210	Thr	Val	Asn	Cys	Ala 215	Arg	Leu	Leu	Lys	Ala :220	Asp	His	His	Ala
Thr	Asn	Gly	Val	Val	His	Leu	Ile	Asp	Lys	Val	Ile	Ser	Thr	Ile	Thr
223					230					235					240
				245					250					255	
			260		Ala			265					270		
Gly	Gln	Tyr 275	Thr	Leu	Leu	Ala	Pro 280	Thr	Asn	Glu	Ala	Phe 285	Glu	Lys	Ile
Pro	Ser 290	Glu	Thr	Leu	Asn	Arg 295	Ile	Leu	Gly	Asp	Pro 300	Glu	Ala	Leu	Arg
Asp 305	Leu	Leu	Asn	Asn	His 310			Lys	Ser		Met	Cys	Ala	Glu	
	Val	Ala	Gly	Leu	Ser	Val	Glu	Thr	Leu	315 Glu	Glv	Thr	Thr	T.eu	320 Glu
				325					330					225	
			340		Asp			345					350		
Ser	Asn	Lys 355	Asp	Ile	Leu	Ala	Thr 360		Gly	Val	Ile	His 365	Tyr	Ile	Asp
Glu	Leu 370	Leu	Ile	Pro	Asp	Ser 375	Ala	Lys	Thr	Leu	Phe 380	Glu	Leu	Ala	Ala
Glu 385	Ser	Asp	Val	Ser	Thr		Ile	Asp	Leu	Phe	Arg	Gln	Ala	Gly	Leu
		His	Leu	Ser	390 Gly	Ser	Glu	Arg	Leu	395 Thr	 Leu	Leu	Ala	Pro	400 Leu
				405					410					415	
			420		Asp			425					430		
Asn	Leu	Leu 435	Arg	Asn	His	Ile	Ile 440	Lys	Asp	Gln		Ala 445	Ser	Lys	Tyr

```
Leu Tyr His Gly Gln Thr Leu Glu Thr Leu Gly Gly Lys Lys Leu Arq
    450
                        455
Val Phe Val Tyr Arg Asn Ser Leu Cys Ile Glu Asn Ser Cys Ile Ala
                     470
                                         475
Ala His Asp Lys Arg Gly Arg Tyr Gly Thr Leu Phe Thr Met Asp Arg
                485
                                     490
Val Leu Thr Pro Pro Met Gly Thr Val Met Asp Val Leu Lys Gly Asp
                                 505
Asn Arg Phe Ser Met Leu Val Ala Ala Ile Gln Ser Ala Gly Leu Thr
                            520
                                                 525
Glu Thr Leu Asn Arg Glu Gly Val Tyr Thr Val Phe Ala Pro Thr Asn
                        535
Glu Ala Phe Arg Ala Leu Pro Pro Arg Glu Arg Ser Arg Leu Leu Gly
                    550
Asp Ala Lys Glu Leu Ala Asn Ile Leu Lys Tyr His Ile Gly Asp Glu
                                    570
Ile Leu Val Ser Gly Gly Ile Gly Ala Leu Val Arg Leu Lys Ser Leu
            580
                                585
Gln Gly Asp Lys Leu Glu Val Ser Leu Lys Asn Asn Val Val Ser Val
                            600
                                                 605
Asn Lys Glu Pro Val Ala Glu Pro Asp Ile Met Ala Thr Asn Gly Val
                        615
                                             620
Val His Val Ile Thr Asn Val Leu Gln Pro Pro Ala Asn Arg Pro Gln
                    630
                                        635
Glu Arg Gly Asp Glu Leu Ala Asp Ser Ala Leu Glu Ile Phe Lys Gln
                                    650
Ala Ser Ala Phe Ser Arg Ala Ser Gln Arg Ser Val Arg Leu Ala Pro
                                665
Val Tyr Gln Lys Leu Leu Glu Arg Met Lys His
                            680
      <210> 123
```

<211> 1205

<212> DNA

<213> Homo sapien

<400> 123

ccagtcagca gagggacagg aatcattcgg ccactgttca gacgggagcc acacccttct 60 ccaatccaag cctggcccca gaagatcaca aagagccaaa gaaactggca ggtgtccacg 120 cgctccaggc cagtgagttg gttgtcactt actttttctg tggggaagaa attccatacc 180 ggaggatgct gaaggctcag agcttgaccc tgggccactt taaagagcag ctcagcaaaa 240 agggaaatta taggtattac ttcaaaaaaag caagcgatga gtttgcctgt ggagcggtgt 300 ttgaggagat ctgggaggat gagacggtgc tcccgatgta tgaaggccgg attctgggca 360 aagtggagcg gatcgattga gccctgcggt ctggctttgg tgaactgttg gagcccgaag 420 ctcttgtgaa ctgtcttggc tgtgagcaac tgcgacaaaa cattttgaag gaaaattaaa 480 ccaatgaaga agacaaagtc taaggaagaa tcggccagtg ggccttcggg agggcggggg 540 gaggttgatt ttcatgattc atgagctggg tactgactga gataagaaaa gcctgaacta 600 tttattaaaa acatgaccac tcttggctat tgaagatgct gcctgtattt gagagactgc 660 catacataat atatgacttc ctagggatct gaaatccata aactaagaga aactgtqtat 720 agcttacctg aacaggaatc cttactgata tttatagaac agttgatttc ccccatcccc 780 agtttatgga tatgctgctt taaacttgga agggggagac aggaagtttt aattgttctg 840 actaaactta ggagttgagc taggagtgcg ttcatggttt cttcactaac agaggaatta 900 tgctttgcac tacgtccctc caagtgaaga cagactgttt tagacagact ttttaaaatg 960 gtgccctacc attgacacat gcagaaattg gtgcgttttg ttttttttc ctatgctgct 1020 ctgttttgtc ttaaaggtct tgaggattga ccatgttgcg tcatcatcaa cattttgggg 1080

```
gttgtgttgg atgggatgat ctgttgcaga gggagaggca gggaaccctg ctccttcggg
                                                                        1140
 ccccaggttg atcctgtgac tgaggctccc cctcatgtag cctccccagg cccagggccc
                                                                        1200
                                                                        1205
        <210> 124
        <211> 583
        <212> DNA
        <213> Homo sapien
       <400> 124
 ccaagaagca gtggccttat tgcatcccaa accacgcctc ttgaccaggc tgcctccctt
                                                                         60
 gtggcagcaa cggcacagct aattctactc acagtgcttt taagtgaaaa tggtcgagaa
 agaggcacca ggaageegte etggegeetg geagteegtg ggaegggatg gttetggetg
                                                                        120
 tttgagattc tcaaaggagc gagcatgtcg tggacacaca cagactattt ttagattttc
                                                                        180
 ttttgccttt tgcaaccagg aacagcaaat gcaaaaactc tttgagaggg taggagggtg
                                                                        240
 ggaaggaaac aaccatgtca tttcagaagt tagtttgtat atattattat aatcttataa
                                                                        300
                                                                        360
 ttgttctcag aatcccttaa cagttgtatt taacagaaat tgtatattgt aatttaaaat
 aattatataa ctgtatttga aataagaatt cagacatctg aggttttatt tcattttca
                                                                        420
                                                                        480
 atagcacata tggaattttg caaagattta atctgccaag ggccgactaa gagaagttgt
                                                                        540
 aaagtatgta ttatttacat ttaatagact tacagggata agg
                                                                        583
       <210> 125
       <211> 783
       <212> DNA
       <213> Homo sapien
       <400> 125
tcaaccatac atactgcttc cactagctaa taccaaatgc aggttctcag atccagacaa
                                                                         60
atggaggaaa agaacattta tgcttccgtt tcagaaagcc aagtcgtagt tttggccctt
cctttctcta aagtttattc ccaaaaacag gtagcattcc tgattgggca gagaagagga
                                                                        120
tattttcagc ccacatctgc tgcaggtatg tcattttctc ccatcttcac tgtgactagt
                                                                        180
aaagatctca ccacttctct ttggaatttc caactttgct tgtgattgaa tgtcacttcg
                                                                        240
                                                                        300
tgaatttgta ttatgtcaga tcacttggca ttgctcttcc atatgcatca agttgccagg
cactgttgcg ctgtcgggcc cactggaatc cacgggggtg aaacaaattc aattatgctt
                                                                       360
                                                                       420
ttacagatcc tgctcaaaaa aggtttcaac tgcttaacca agtacagctc attcttccac
cttcttactc tgcaaccaaa ccaagtgccc catactacag gtaggtgccg agaaattccg
                                                                       480
cagcagaaaa tccaaaatca tttctgaaac ctccttgcta acaaaagttc ttttttctc
                                                                       540
                                                                       600
caaacagcat ataaaatgat caagtcttga aagagaaaag aagcaaagta gcaaatacat
caacaattca ctatcagaaa cacataaaat cccagagaga gagaaggcag tatctctgaa
                                                                       660
                                                                       720
tcatggatgg acttggaaag ttcggaagga ttccgagtgc ttcctttcag aaagacaatt
                                                                       780
ctq
                                                                       783
      <210> 126
      <211> 604
      <212> DNA
      <213> Homo sapien
      <400> 126
cctgctagaa tcactgccgc tgtgctttcg tggaaatgac agttccttgt tttttttgtt
                                                                     ....60
totgtttttg ttttacatta gtcattggac cacagocatt caggaactac cocctgecce
acaaagaaat gaacagttgt agggagaccc agcagcacct ttcctccaca caccttcatt
                                                                       120
                                                                       180
ttgaagttcg ggtttttgtg ttaaagttaa tctgtacatt ctgtttgcca ttgttacttg
                                                                       240
tactatacat ctgtatatag tgtacggcaa aagagtatta atccactatc tctagtgctt
gactttaaat cagtacagta cctgtacctg cacggtcacc cgctccgtgt gtcgccctat
                                                                       300
                                                                       360
attgagggct caagctttcc cttgtttttt gaaaggggtt tatgtataaa tatattttat
                                                                       420
```

```
gcctttttat tacaagtctt gtactcaatg acttttgtca tgacattttg ttctacttat
                                                                     480
actgtaaatt atgcattata aagagttcat ttaaggaaaa ttacttggta caataattat
                                                                     540
600
aaaa
                                                                     604
     <210> 127
     <211> 417
      <212> DNA
     <213> Homo sapien
     <400> 127
ctgagectet gteaccagag aaggetgagg ceceaatgge acaceteaga aacetacace
                                                                      60
ccgaggctgg acggctggac tcctgagcac aagctccctc tcgcaccctt tgccagacag
                                                                     120
tttgtctcca atttcaaact gacctaaggc tcttactcct ggattttttg tttttaaacc
                                                                     180
ttctcccagc cagtcttcgg gagggcatga ttagagaagt gctcctttgc tgatggagga
                                                                     240
ggggacctaa ggaagaaggt ggatcccagg tgcctcctct ctaattgatc ctccccacct
                                                                     300
agtiticetti geetetette ettetaeeag gieatgitti itaetetetg eecettetge
                                                                     360
ctcctagcat ttcaaaaact gtagagtgca ccccatagtg gacattttta gtccagg
                                                                     417
     <210> 128
     <211> 657
     <212> DNA
     <213> Homo sapien
      <400> 128
ccacactgaa atgcagttta atgtggaaac ttttctaaat acatattgta gcatctttgg
                                                                      60
acatcaacgt gtggcctgaa atttttatta ttgttccctc ttctcctcca ttaaaaaaaa
                                                                     120
aatctccttg tggtatttag tcatttacca ttaacacata ttatggctta aaaagggcca
                                                                     180
tcccttcctt ttctgagctg gagttcttca cgctcacctt tgatgcatgg ccttagctgg
                                                                     240
ttactttgcc ttggtttggt catgaacatt ggggttagtg gcctggcaac ttgaatgcat
                                                                     300
atggaaagaa caatgccaag tgatctgaca taatacaaat tccgaagtga cattcaatca
                                                                     360
caagcaaagt tggaaattcc aaagagaagt ggtgagatct ttactagtca cagtgaagat
                                                                     420
gggagaaaat gacatacctg cagcagatgt gggctgaaaa tatcctcttc tctgcccaat
                                                                     480
caggaatgct acctgttttt gggaataaac tttagagaaa ggaagggcca aaactacgac
                                                                     54.0
ttggctttct gaaacggaag cataaatgtt cttttcctcc atttgtctgg atctgagaac
                                                                     600
ctgcatttgg tattagctag tggaagcagt atgtatggtt gaagtgcatt gctgcag
                                                                     657
      <210> 129
      <211> 1220
      <212> DNA
      <213> Homo sapien
      <400> 129
cgcgtgctcg gctcacacca acaaggcaag ccaaaggcgc ccctccccag agggatccct
                                                                      60
aacgtgccca gcatgtagat tctggactaa cagacaacat acattcaccg ctggtcaccc
                                                                     120
agatecteat teaaaceeae tgetggeaea teeettteet taetttgeee tgtgetaeea
                                                                     180
gccacggaag gagcctctct tgttttttct ataaaatggg taggcaggag aaaagcaggt
                                                                     240
gccctaagat tgctctaagg cccagcatgt ggttacagtt ctctgacttg cagaacctgc
                                                                     300
                                                                    *3.60
caggtgtatg gctacaagtt atcctcgtgc"tgatctgtct cattactaag ttaatggaga
agacagaaag gtaaaaatca cgtgtagcaa gaacaactct tatttcacaa actcaggtat
                                                                     420
gaaacgaaac gcctgtcctt catggaactg cttttagctc ctgtcttttc aaaatggcag
                                                                     480
agggagttcc tacacacact ttttccctgg aggccaaggt ctaggggtag aaaggggagg
                                                                     540
ggtggggcta ccaggtagca gttgacaacc caaggtcaga ggagtggccc tcagtgtcat
                                                                     600
ctgtccacag tgatacctgc caagatgacc actgacccac atctggtctt agtcattggt
                                                                     660
ctcctcagat ttctggggcc acctgcaagc cccattccat tcctacagat ctctcagcca
                                                                     720
```

```
cctgtaagtc ctttgtgaag atgtgggtga cacaggggga caggaaaacc catttctcaa
                                                                        780
 cccagatcca tgtctccact gcttctactc tgggttggga ttcaggaaga caggcacagt
                                                                        840
 cctctctgtt catagaaaca cctgccagtg tcaaggattc cagtcaggtg tctatcccaa
                                                                        900
 ctggtcaggg agagaagggc agacccattc tcaaagacca ccatgtccaa ggtctgacag
                                                                        960
 ctccccactg gctgcccca caggggcttt aggctggtct gggtcatggg gaagcgtccc
                                                                       1020
 tcttatcgct ggtctgtgtt ctcctggatt tggtatctat gttggtacga ctcctggcct
                                                                       1080
tttatctaaa ggactttggc ttttgtaaat cacaagccaa taatagactt ttttctcccc
                                                                       1140
ctctgttttt tgctgtgtca tctctgcctt gagactgcct tgagacagtg cttgccttga
                                                                       1200
 gagagtgagc caattaacag
                                                                       1220
       <210> 130
       <211> 1274
       <212> DNA
       <213> Homo sapien
       <400> 130
ccatatgagt ttgccatctc catggatgcc atttcaatgc cttcagggta atcattctct
                                                                         60
ccccaaagac tgcccacggg gtcatcactc ctgtgacgaa atgagggctg gattgaagat
                                                                        120
gttctgctga gcaccccct ggtcatcttt ggggtctcag aagagccata atcatgacca
                                                                        180
ttctcagcat ctgaataatc aggttctctc caagtgcttg gcaagttctg attgtcctca
                                                                        240
gcactgggat agtctggctc cccaaaaaag ggtggagagt taggttgaat gtcagcgcct
                                                                        300
ggataatcag gctttcccag agagtctgcg tatggattga ttctaaaact tgtatgttcc
                                                                       360
agattettte tggateetgg atggtteaaa ttggetetgg gteeaggatg ateagagttg
                                                                       420
ctctgagctc cagggtagtc cggttctaag gagccaaaat gatctggatg tgttctggag
                                                                       480
cctgcatagt ttccactgct gctggagcct gcaaaatcag gatttcgttg agatccaggg
                                                                       540
tagtorggtt gtorggatga tgoroggtgg tagggatgac torgaaatto actataatot
                                                                       600
ggctctggta gagaggtagg atggtctggg cttgttctag aggctgcaga gtatgcattg
                                                                       660
cttctggtgc cagaatagtc tggattactc agagatctag gataatttgg ttctgccaga
                                                                       720
gacccaggat agtctggacg tgttctggag gctacagagt atggattgct cctggtgccg
                                                                       780
gggtaatctg gattgttcag aggacctgga acatctggat aaccttgagt tttcaaatac
                                                                       840
ccctgcgtac ggttctgaga ccctgaatag tcagggtaat ctgggtcttc ctcagaccag
                                                                       900
ttattcctgt agtaggcaga catgttggta tggactcttc accctggagt ggtaaactgt
                                                                       960
cccagcattt gcaattactc agggatcttt tttttttcac ttttttgccc ttattgttct
                                                                      1020
tgctttgtcc caagtagatg caaatgttgt gcaaaccaac ttgatcttaa gatgttgtta
                                                                      1080
agaacactgg agtcacgtgt ccatgggtcc ttcaggctgg cttttgatgg gagctgggat
                                                                      1140
gcagatgatt tacggagggt tataatctgt gatgctggtc tgaagtctga atattccaag
                                                                      1200
ttgctgactg caggcagagc ctcatgtcct cctggcgctc ctgttgccgc tgcttgcgct
                                                                      1260
ggccctcggg tcga
                                                                      1274
      <210> 131
      <211> 554
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(554)
      <223> n = A,T,C or G
      <400> 131
ctgtaattct gccttttcta ccttcattcc atccttcctc tgcccagata aagkccagca
                                                                        60
gaaattcctc ctttctacct ctctgggact ctgagacagg aaatcttcaa ggaggagttt
                                                                       120
ttccctcccc actattctta ttctcaaccc ccagaggaac caaggctgct gtacccacct
                                                                       180
cagggacaga actccacact atagtgggaa agcttcaggg acccctcctt ttagtgctca
                                                                       240
gggctcacct atgctactgg tccttttggc aaaaaaggaa aatgatagag ccagggttgc
                                                                       300
```



ccctgatgta gcagccttac tgt agggaggtga taaggtgtca tgc ttggggtgag ggaaaccaag tag tacccatagc tagctttctg ccc gccacaggca gcag <210> 132 <211> 787	egttetge tgaacceact ggggttgg agaaggagca	ggntggtatg gcacctttgt	aacatgaggc macacctggc	360 420 480 540 554		
<212> DNA <213> Homo sapien						
<400> 132						
ctggtcaccc aactcttgtg gaa gaggctggaa teettcagec cca ctgcccaggg gtcagggcag tgg ggcatctttg ttteetggtg ccc tagaagtagg getgeteett ttg	agagccca gggaccactc ggtatcac tggtgacatc ctcctcaa agttgctgac ggagctgg agggaataga	cagtagatgc aagaatatca actttgggga cctggagaca	agagagggc gggctgggga cgggaagggg gagttgaggc	60 120 180 240 300		
agtogggotg todaggttot aag agcoagagga todagcoto otd ogcatogatt ttgtggaagt caa gtacotttto acctocacac ttg	cctccctc aaatgtcagt attagaga tgtggggagc	ccaagcaaat tatcggagac	accaaagcaa aagcactatt	360 420 480 540		
cacgcctgcc atggcttgag ctg gactggttgc gcacttgcta agg ataaacaggt ggacttataa tca ttctcatttg tataattgtc tgg cctccag	ggggtgag gagtggtett ggcaggaa gtetggaggg atcatgca etgcaattgt	tatcttcttt ctgcaggaat agaacatagt	gggagateet ggtgeegttg eteetgeett	600 660 720 780 787		
<210> 133 <211> 219 <212> DNA <213> Homo sapien						
<220> <221> misc_feature <222> (1)(219) <223> n = A,T,C or G						
<pre><400> 133 tactgctcta agttttgtna aa aggaaggtca tttccatgta tg aacattggaa gcaggttaaa tg agaattggaa nagactaata tc</pre>	cataataa tcctgcaaag ttttgtaa actttgaaat	tacaggtact	ttgtctaaga	60 120 180 219		
<210> 134 <211> 234 <212> DNA <213> Homo sapien						
<400> 134 gattttaaaa acatcatgac tt taatatgaat gaactccaac tc ttagtaattc acatttaagc aa acttagtgca tattttaatg gt	catttgaa aacatgtgaa gttagcgc cttgctgaat	tcaaagtaca acagcctttg	gttttagaag taaaaaagag	60 120 180 234		

<210> 135

```
<211> 414
       <212> DNA
       <213> Homo sapien
       <400> 135
 ctccagcctg gctatatccg gtcccgctat aacctgggca tcagctgcat caacctcggg
                                                                         60
 gctcaccggg aggctgtgga gcactttctg gaggccctga acatgcagag gaaaagccgg
 ggcccccggg gtgaaggagg tgccatgtcg gagaacatct ggagcaccct gcgtttggca
                                                                        120
                                                                        180
 ttgtctatgt taggccagag cgatgcctat ggggcagccg acgcgcggga tctgtccacc
                                                                        240
 ctcctaacta tgtttggcct gccccagtga cagtgggacg ggctgccctg tgagtgtcca
                                                                        300
 cctggggatt aaatatgtct tcaacaaggg aggcctggct tctacaatgg tttaggtaaa
                                                                        360
 ggggcctttg aagtagttet ggccaggett gcaatacaca caacacaaga gcca
                                                                        414
       <210> 136
       <211> 461
       <212> DNA
       <213> Homo sapien
       <400> 136
 gaagtgatta ataggtttat ttgcatatac acagagaaga gtcagcattg ttgggtgaga
                                                                         60
 agaggcaggc tgtgaggagg taaggcttca gcagaggaag gcaccttgac agacaacacg
                                                                        120
 agactcctat taaatcagca cagttgcaaa cttcacctgc ctcaagccaa cagctcattg
                                                                       180
aactcatatg tcgattgaga atcatttaca aaaccaggag agaaacaatg ggaagagcaa
                                                                       240
cggtctctca tccctggacc tgacactcaa aacattatgt acaggatgca ggaacaaaat
                                                                       300
ctgtctgatc agtgccctct cctgctggga aaaacaccca tcacggaaga atttggggat
                                                                       360
taaatatgtc ttcaacaagg gaggcctggc ttctacaatg gtttaggtaa aggggccttt
                                                                       420
gaagtagttc tggccaggct tgcaatacac acaacacaag a
                                                                       461
       <210> 137
       <211> 269
       <212> DNA
       <213> Homo sapien
      <400> 137
atagcaaatg gacacaaatt acaaatgtgt gtgcgtggga cgaagacatc tttgaaggtc
                                                                        60
atgagtttgt tagtttaaca tcatatatt gtaatagtga aacctgtact caaaatataa
                                                                       120
gcagcttgaa actggcttta ccaatcttga aatttgacca caagtgtctt atatatgcag
                                                                       180
atctaatgta aaatccagaa cttggactcc atcgttaaaa ttatttatgt gtaacattca
                                                                       240
aatgtgtgca ttaaatatgc ttccacagt
                                                                       269
      <210> 138
      <211> 452
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(452)
      <223> n = A,T,Coor G
      <400> 138
ctccatggga ggcaaaatat agagaattta tggtgcccaa ctcttatgta atcactggac
                                                                       60
taatcttccc tggtaactat gcaacatttg gacagaaagg cacacaaaaa agtttaaata
                                                                      120
tttcatgtgc caatctggaa aaaaataatt taaatcaaca gaacagacag tacatctaca
caaatgagga aagcagaaaa gatacctcac attcatttat ctcaggtttc aaagtggctt
                                                                      180
                                                                      240
```



caatgctaaa gtaaatgtat taacatttgg aaaatacaag acaattttt tgtttgtttt caatttttt agctctatac aatgattaca acataagaca aaaaaaaaaa	300 360 420 452
<210> 139 <211> 474 <212> DNA <213> Homo sapien	
<pre><400> 139 tgtgcctcat tgaggttaca attgaaacag atgtgagcac ctgagagact ttccctgatt atattcctcc acaaaccact gtaccatatt accttattt atcttcttga aattcttatt cattggcttg tttgttgtct ctttgcatta gatatatgta agctccttgg cataaatttg acattggtag gggactgaca ttctaacctg gcccaggccc taggagagag ataactccac aaagcagcac atactatctt aggttagcag ggagctaact caccatgtag cagatgaaaa aaaccaaacc cagcactgtg cataaatacc acttgccaag aagtcaggtc ctcggcaacc gagaatcaac ctcagcacaa acgcaggtgg ctgggctctg ttccccctta gccaccacct cagcctctcc cctccctgc cccaagtgcc caagagcttg gctctctgtg cttt</pre> <210> 140	60 120 180 240 300 360 420 474
<210> 140 <211> 487 <212> DNA <213> Homo sapien	
<pre><400> 140 cttccctgcc tcgtgttcct gagaaacgga ttaatagccc tttatccccc tgcaccctcc tgcaggggat ggcactttga gccctctgga gccctccct tgctgagcct tactctctc agactttctg aatgtacagt gccgttggtt gggatttggg gactggaagg gaccaaggac actgaccca agctgtcctg cctagcgtcc agcgtcttct aggagggtgg ggtctgcctg tcctggtgtg gttggtttgg ccctgtttgc tgtgactacc ccccccctc cccgaaccga gggacggctg cctttgtctc tgcctcagat gccacctgcc ccgcccatgc tccccatcag cagcatccag actttcagga agggcagggc cagccagtcc agaaccgcat ccctcagcag ggactgataa gccatctctc ggagggccc ctaataccca agtggagtct ggttcacacc ctggggg</pre>	60 120 180 240 300 360 420 480 487
<210> 141 <211> 248 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(248) <223> n = A,T,C or G	
<pre><400> 141 ttaaagatgg ggaaatgagg cctgnaaata gaaaagattt gcctagagtc acacacactg tcaggtcagg tagagtcaaa atcaggcacc ccgactcaca gactgcttca cattgccatc ** agagattgtc ctgcaacaat attatgttta gttctactgc agaatgataa ctggatctta ccccctttgc ctgatctggc cacaaacttg tttttcaggt ctttccatta ggctctctc agctaatt</pre>	60 120° 180 240 248
<210> 142	

<211> 173

```
<212> DNA
       <213> Homo sapien
       <400> 142
tactaagatt gtccaagcct ccctcttaaa actttctttc cctttagagg aatcattact
                                                                        60
tegtattaaa agtttetaet teettgtaga atatetaeat eeaatgggee atggeacaaa
                                                                       120
atttaagtct agaaagaatc ttaaaggctc atcttatagt aaccagaggc agg
                                                                       173
      <210> 143
      <211> 511
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(511)
      <223> n = A,T,C or G
      <400> 143
cctcgtcaga ggggtggttc ctggtnacct gtactccacg gacctcggtg aagcaaaagc
                                                                        60
ttcagggcag agggaatgag gcaacccagt ggcagccccg ctgggccccg tggctcctgc
                                                                       120
tctcctattg gacgtagagg caggggagag acttctctat acaaatattc tcatcacaga
                                                                       180
agggatgate ettgetgete tgeegtaggg tttttgatge tgagetatge tgeacatgae
                                                                       240
gttaacctaa agaacttgga ctgagctttt aaaaaaggac agcaaacaat tttataatcc
                                                                       300
ttaaagtgta atagacggtt acactagtgc agggtattgg ggaggctctt tgggtgtgga
                                                                       360
ggctgtcact tgtatttatt gtgactctaa atctttgata gtaaaacaaa tgtaaaaaga
                                                                       420
aatgtttgcc accagatggg aatagaagtt ccaataagca ggctggaatg ggtggctata
                                                                       480
cgttgtatca cgaggaagtt ttagactctg a
                                                                       511
      <210> 144
      <211> 190
      <212> DNA
      <213> Homo sapien
      <400> 144
cattettetg teacatgeea atteagttgt caateceatt gtetatgett accggaaccg
                                                                       60
agactteege tacactttte acaaaattat etecaggtat ettetetgee aageagatgt
                                                                      120
caagagtggg aatggtcagg ctggggtaca gcctgctctc ggtgtgggcc tatgatctag
                                                                      180
gctctcgcct
                                                                      190
      <210> 145
      <211> 169
      <212> DNA
      <213> Homo sapien
      <400> 145
gatgtggtta tctcctcaga tggccagttt gccctctcag gctcctggga tggaaccctg
                                                                       60
cgcctctggg atctcacaac gggcaccacc acgaggcgat ttgtgggcca taccaaggat
                                                                      120
gtgctgagtg tggccttctc ctctgacaac cggcagattg tctctggat
                                                                      169
      <210> 146
      <211> 511
      <212> DNA
      <213> Homo sapien
```

```
<400> 146
atctagagaa gatttgggaa acacatgata gctatggtta aatacttaac agggcaatca
                                                                        60
cagggaagat gactagattt cctaacatcc atgagtgaaa tttatagaag tatactctct
                                                                       120
gacttgatat aaaggaagat tttaaaaaaac atgactgttc aggagtgttc aagtagggtc
                                                                       180
agatgaccag tgattgggaa tacttcgtaa gcaggagcaa gtaagatctg agccactgtt
                                                                       240
ctatcggtag ggtgtctgtg gtattccttg gtcaaagaag tactctaagc aacttcagtc
                                                                       300
tcacgaatta ctatcaccct cgtgggcata catgatggtt accctaaaga ggaagtttca
                                                                       360
gaaggcagta atattggatc ctggaatagt cagacaggag ccttcatgca gatacccttt
                                                                       420
tragttetre atacacerat tracaagtgg tracaaaaar accragtare tttacttgge
                                                                       480
tttacccact taacaatatg ctcaatatga g
                                                                       511
      <210> 147
      <211> 421
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(421)
      <223> n = A, T, C or G
      <400> 147
gaccagttga gttcttcctg gctattgtat aatccacagc cacactgtga aagcaaatct
                                                                        60
ggccagttag caacacaggg agaatctgcc tgaactgacc aaaggtgtcc atacttcatg
                                                                       120
tcagtgagaa tttcacctcc atcatgttct aaagagccaa caacagattc tagggcactg
                                                                       180
caaaatgctt cagcaattaa ttgaagttct gtttgagtac attcatcatc tttgagaatg
                                                                       240
ctttctgggt cgttgtgagt cttgtgtctg atatatgcag ccaaatgagt ttcagtacag
                                                                       300
ccacctccca acaaagccca tggttccttg agtgttaact gcaggacatg cagtgccgtc
                                                                       360
tgacacgtga gcttcagctc atcccangca gtgtcatttc tgttgcagag aagccaagct
                                                                       420
                                                                       421
      <210> 148
      <211> 237
      <212> DNA
      <213> Homo sapien
      <400> 148
acacaccact gttggccttc catctgggtt aagtcaactg tgagtagaaa ccgaagataa
                                                                        60
cagttttgta ttcataatgq ccttttcata ctccaaqtac ttttqaqcac aqaqcctctt
                                                                       120
gcttctgacc tggcacttgg aacacagata tatatatctt ttgttctgtc cctgggaaac
                                                                       180
tgatatttgt gtaagacaac caccagatat tttctctaat aaaatcttct aaaatta
                                                                       237
      <210> 149
      <211> 168
      <212> DNA
      <213> Homo sapien
      <400> 149
agagaaagtt aaagtgcaat aatgtttgaa gacaataagt ggtggtgtat cttgtttcta ~
                                                                      - 60
ataagataaa cttttttgtc tttgctttat cttattaggg agttgtatgt cagtgtataa
                                                                       120
aacatactgt gtggtataac aggcttaata aattctttaa aaggagag
                                                                       168
      <210> 150
      <211> 68
```

<212> DNA

```
<213> Homo sapien
                <220>
                <221> misc_feature
                <222> (1)...(68)
                <223> n = A,T,C or G
                <400> 150
  ggtggggttt ggcagagatg antttaagtg ctgtggccag aagcgggggg ggggtttggt
                                                                                                                                                                   60
  ggaaattt
                                                                                                                                                                   68
                <210> 151
                <211> 421
                <212> DNA
                <213 Homousapien was a series of the series 
                <400> 151
 aggtgacacg tattcgggat gaaagtataa tagtcattcc ttcaaccctt gcatttatgg
                                                                                                                                                                  60
 actotggaaa togaagatoo acagtgagta aagatgttog tocaaagaca aaaaatagaa
                                                                                                                                                                120
 acageteaae aaagegagag acaaaaaae aaaatggeae tgtggetetg eetttgaagt
                                                                                                                                                                180
 ctgggctcca gcagagggct gatcttccca caggagacga gacggcctat gacactctcc
                                                                                                                                                                240
 agaactgttg tcagtgccga attttacttc ccttgcccat tctaaatgag caccaggaga
                                                                                                                                                                300
 agtgccagag gttagctcac caaaagaaac tccagtgggg ctggtgagat ggctcagcgg
                                                                                                                                                                360
 gtaagagcac ccgactgctc ttccgaaggt ccggagttca aatcccagca accacatggt
                                                                                                                                                                420
                                                                                                                                                                421
               <210> 152
               <211> 507
               <212> DNA
               <213> Homo sapien
              <220>
               <221> misc feature
               <222> (1)...(507)
              <223> n = A, T, C or G
              <400> 152
gaatteggea enagetegtg eegeeagggt nggteenttt tttgeteege etegeeanga
                                                                                                                                                                60
cttcctacag ctatcgccag tcgtcggcca cgtcntcctt cngaggcctg ggcggcggct
                                                                                                                                                               120
ccgtgcgttn tgggccgggg gtcgcctttc nctcncccag cattcacggg ggctccggcg
                                                                                                                                                               180
gccgcggcgt atccgtgtcc tccgcccgct ntgtgtcctc gtcctcctcn ggggcctacg
                                                                                                                                                               240
gctngctgct acngcggctt cctgaccgct tccnacgggc tgctggcngg caacgagaag
                                                                                                                                                               300
ctaaccatgc agaacctnaa cnaccgcctg gcctcctacc tgnacaaggt gcgcnccctg
                                                                                                                                                               360
taggcggcca acggcnagct agaggtgaag atccnctact gggtaccaga agcaggggcc
                                                                                                                                                               420
tgggccctgc ccgactacag ccactnctnc acnaccatgc agtacctgcn ggganaagat
                                                                                                                                                               480
tntngggngc caccatngag aactgca
                                                                                                                                                               507
              <210> 153
              <211> 513
              <212> DNA
              <213> Homo sapien
             <400> 153
gaattcggca cgaggtggct cagatgtcca ctactgggag tatggtcgaa ttgggaattt
                                                                                                                                                                60
tattgtgaaa aagcccatgg tgctgggaca tgaagcttcg ggaacagtcg aaaaagtggg
                                                                                                                                                              120
```



```
atcatcggta aagcacctaa aaccaggtga tcgtgttgcc atcgagcctg gtgctccccg
                                                                       180
agaaaatgat gaattetgea agatgggeeg atacaatetg teacetteea tettettetg
                                                                       240
tgccgcgccc cccgatgacg ggaacctctg ccggttctat aagcacaatg cagccttttg
                                                                       300
ttacaagctt cctgacaatg tcacctttga ggaaggcgcc ctgatcgagc cactttctgt
                                                                       360
ggggatccat gcctgcagga gaggcggagt taccctggga cacaaggtcc ttgtgtqtqq
                                                                       420
agctgggcca atcgggatgg tcactttqct cgtggccaaa gcaatgggag cagctcaaqt
                                                                       480
agtggtgact gatctgtctg ctacccgatt gtc
                                                                       513
      <210> 154
      <211> 507
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(507)
      <223> n = A,T,C or G
      <400> 154
ggcacgagct cgtgccgaat tcggcncgag cagacacaat ggtaagaatg gtgcctgtcc
                                                                        60
tgctgtctct gctgctgctt ctgggtcctg ctgtccccca ggagaaccaa gatgqtcqtt
                                                                       120
actictictgac ctatatictac actgggctgt ccaagcatgt tgaagacgtc cccgcgtttc
                                                                       180
aggcccttgg ctcactcaat gacctccagt tctttagata caacagtaaa gacaggaagt
                                                                       240
ctcagcccat gggactctgg agacaggtgg aaggaatgga ggattggaag caggacagcc
                                                                       300
aacttcagaa ggccagggag gacatcttta tggagaccct gaaagacatc gtggagtatt
                                                                       360
acaacgacag taacgggtct cacgtattgc agggaaggtt tggttgtgag atcgagaata
                                                                       420
acagaagcag cggagcattc tggaaatatt actatgatgg aaaggactac attgaattca
                                                                       480
acaaagaaat cccagcctgg gtcccct
                                                                       507
      <210> 155
      <211> 507
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(507)
      <223> n = A,T,C or G
      <400> 155
ggcacgagga gacctaaggg ctgagtntcg ggaacaggag aaagctctgt tggccctcca
                                                                        60
gcagcagtgt gctgagcagg cacaggagca tgaggtggag accagggccc tgcaggacag
                                                                       120
ctggctgcag gcccaggcag tgctcaagga acgggaccag gagctggaag ctctgcgggc
                                                                       180
agaaagtcag tcctcccggc atcaggagga ggctgcccgg gcccgggctg aggctctgca
                                                                       240
ggaggccctt ggcaaggctc atgctgccct gcaggggaaa gagcagcatc tcctcgagca
                                                                       300
ggcagaattg agccgcagtc tggaggccag cactgcaacc ctgcaagcct ccctggatgc
                                                                       360
ctgccaggca cacagtcggc agctggagga ggctctgagg atacaagaag gtgagatcca
                                                                       420
ggaccaggat ctccgatacc aggaggatgt gcagcagctg cagcaggcac ttgcccagag
                                                                       480
ggatgaagag ctgagacatc agcagga
                                                                       507
      <210> 156
      <211> 509
      <212> DNA
      <213> Homo sapien
```

```
<220>
        <221> misc_feature
        <222> (1)...(509)
        <223> n = A,T,C or G
        <400> 156
 ggcacgagga cagagagaac cctgtngaaa gagcgttacc aggaggtcct ggacaaacag
 aggcaagtgg agaatcagct ccaagtgcaa ttaaagcagc ttcagcaaag gagagaagag
                                                                          60
 gaaatgaaga atcaccagga gatattaaag gctattcagg atgtgacaat aaagcgggaa
                                                                         120
 gaaacaaaga agaagataga gaaagagaag aaggagtttt tgcagaagga gcaggatctg
                                                                         180
 aaagctgaaa ttgagaagct ttgtgagaag ggcagaagag aggtgtggga aatggaactg
                                                                         240
 gatagactca agaatcagga tggcgaaata aataggaaca ttatggaaga gactgaacgg
                                                                        300
 gcctggaagg cagagatett atcactagag agccggaaag agttactggt actgaaacta
                                                                        360
 gaagaagcag aaaaagaggc agaattgcac cttacttacc tcaagtcaac tcccccaaca
                                                                        420
 ctggagacag ttcgttccaa acaggagtg
                                                                        480
                                                                        509
       <210> 157
       <211> 507
       <212> DNA
       <213> Homo sapien
       <400> 157
 ggcacgaggg cagecetect accggegeac gtggtgeege egetgetgee teeegetege
 cctgaaccca gtgcctgcag ccatggctcc cggccagctc gccttattta gtgtctctga
                                                                         60
caaaaccggc cttgtggaat ttgcaagaaa cctgaccgct cttggtttga atctggtcgc
                                                                        120
ttccggaggg actgcaaaag ctctcaggga tgctggtctg gcagtcagag atgtctctga
                                                                        180
gttgacggga tttcctgaaa tgttgggggg acgtgtgaaa actttgcatc ctgcagtcca
                                                                        240
tgctggaatc ctagctcgta atattccaga agataatgct gacatggcca gacttgattt
                                                                        300
caatettata agagttgttg cetgeaatet etateeettt gtaaagacag tggettetee
                                                                        360
aggtgtaagt gttgaggagg ctgtggagca aattgacatt ggtggagtaa ccttactgag
                                                                        420
                                                                       480
agctgcagcc aaaaaccacg ctcgagt
                                                                       507
      <210> 158
      <211> 507
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(507)
      <223> n = A, T, C or G
      <400> 158
ggcacgagtc gagctgtgcc tattcgngtc aatccaagag tgagtaatgt gaagtctgtc
tacaaaaccc acattgatgt cattcattat cggaaaacgg atgcaaaacg tctgcatggc
                                                                        60
cttgatgaag aagcagaaca gaaacttttt tcagagaaac gtgtggaatt gcttaaggaa
                                                                       120
ctttccagga aaccagacat ttatgagagg cttgcttcag ccttggctcc aagcatttat
                                                                       180
gaacatgaag atataaagaa gggaattttg cttcagctct ttggcgggac aaggaaggat
                                                                       240
tttagtcaca ctggaagggg caaatttcgg gctgagatca acatcttgct gtgtggcgac
                                                                      300
cctggtacca gcaagtccca gctgctgcag tacgtgtaca acctcgtccc caggggccag
                                                                      360
tacacgining ggaagggcic cagigcanni ggccinacig chiacgiaai gaaagaccci
                                                                      420
gagacaaggn anctggnnct gnnacag
                                                                      480
                                                                      507
     <210> 159
      <211> 508
```

PCT/US99/30909

51

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(508)
      <223> n = A, T, C \text{ or } G
      <400> 159
ggcacnanaa accaggatta tggtnnggat ccaaagattg ctaatgcaat aatgaaqqca
                                                                         60
gcagatgagg tagctgaagg taaattaaat gatcattttc ctctcgtggt atggcagact
                                                                       120
ggatcaggaa ctcagacaaa tatgaatgta aatgaagtca ttagcaatag agcaattgaa
                                                                        180
atgttaggag gtgaacttgg cagcaagata cctgtgcatc ccaacgatca tgttaataaa
                                                                        240
agccagaget caaatgatac ttttcccaca gcaatgcaca ttgctgctgc aatagaagtt
                                                                        300
catgaagtac tgttaccagg actacagaag ttacatgatg ctcttgatgc aaaatccaaa
                                                                        360
gagtttgcac agatcatcaa gattggacgt actcatactc aggatgctgt tccacttact
                                                                        420
cttgggcagg aatttagtgg ttatgttcaa caagtaaaat atgcaatgac aagaataaaa
                                                                        480
getgecatge caagaateta tgageteg
                                                                        508
      <210> 160
      <211> 508
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(508)
      <223> n = A, T, C or G
      <400> 160
ggcacgaget tggagcaaag teatetnaag gaattagagg acacaettea ggttaggeae
                                                                        60
atacaagagt ttgagaaggt tatgacagac cacagagttt ctttggagga attaaaaaag
                                                                       120
gaaaaccaac aaataattaa tcaaatacaa gaatctcatq ctqaaattat ccaqqaaaaa
                                                                       180
gaaaaacagt tacaggaatt aaaactcaag gtttctgatt tqtcaqacac qaqatqcaag
                                                                       240
ttagaggttg aacttgcgtt gaaggaagca gaaactgatg aaataaaaat tttgctggaa
                                                                       300
gaaagcagag cccagcagaa ggagaccttg aaatctcttc ttgaacaaga gacagaaaat
                                                                       360
ttgagaacag aaattagtaa actcaaccaa aagattcagg ataataatga aaattatcag
                                                                       420
gtgggcttag cagagctaag aactttaatg acaattgaaa aagatcagtg tatttccgag
                                                                       480
ttaattagta gacatgaaga agaatcta
                                                                       508
      <210> 161
      <211> 507
      <212> DNA
      <213> Homo sapien
      <400> 161
ggcacgageg ctaceggege etectetgeg gecaetgage eggageegge etgageageg
                                                                        60
eteteggttg cagtacecae tggaaggaet taggegeteg egtggaeaee geaageeeet
                                                                       120
cagtageete ggeccaagag-geetgettte caetegetag eecegeeggg ggteegtgte ** ** 180
ctgtctcggt ggccggaccc gggcccgagc ccgagcagta gccggcgcca tgtcggtggt
                                                                       240
gggcatagac ctgggcttcc agagctgcta cgtcgctgtg gcccgcgccg gcggcatcga
                                                                       300
gactateget aatgagtata gegacegetg caegeegget tgeatttett ttqqteetaa
                                                                       360
gaatcgttca attggagcag cagctaaaag ccaggtaatt tctaatgcaa aqaacacagt
                                                                       420
ccaaggattt aaaagattcc atggccgagc attctctgat ccatttgtgg aggcagaaaa
                                                                       480
atctaacctt gcatatgata ttgtgca
                                                                       507
```

```
<210> 162
      <211> 507
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(507)
      \langle 223 \rangle n = A,T,C or G
      <400> 162
ggcacgagca gctgtgcacc gacatgntct cagtgtcctg agtaagacca aagaagctgg
                                                                         60
caagatcctc tctaataatc ccagcaaggg actggccctg ggaattgcca aagcctggga
                                                                        120
gctctacggc tcacccaatg ctctggtgct actgattgct caagagaagg aaagaaacat
                                                                        180
atttgaccag cgtgccatag agaatgagct actggccagg aacatccatg tgatccgacg
                                                                        240
aacatttgaa gatatctctg aaaaggggtc tctggaccaa gaccgaaggc tgtttgtgga
                                                                        300
tggccaggaa attgctgtgg tttacttccg ggatggctac atgcctcgtc agtacagtct
                                                                        360
acagaattgg gaagcacgtc tactgctgga gaggtcacat gctgccaagt gcccagacat
                                                                        420
tgccacccag ctggctggga ctaagaaggt gcagcaggag ctaagcaggc cgggcatgct
                                                                        480
ggagatgttg ctccctggcc agcctga
                                                                        507
      <210> 163
      <211> 460
      <212> DNA
      <213> Homo sapien
      <400> 163
ggcacgagaa ataactttat ttcattgtgg gtcgcggttc ttgtttgtgg atcgctgtga
                                                                         60
tcgtcacttg acaatgcaga tcttcgtgaa gactctgact ggtaagacca tcaccctcga
                                                                        120
ggttgagccc agtgacacca tcgagaatgt caaggcaaag atccaagata aggaaggcat
                                                                        180
ccctcctgac cagcagaggc tgatctttgc tggaaaacag ctggaagatg ggcgcaccct
                                                                        240
gtctgactac aacatccaga aagagtccac cctgcacctg gtgctccgtc tcagaggtgg
                                                                        300
gatgcaaatc ttcgtgaaga cactcactgg caagaccatc acccttgagg tggagcccag
                                                                       360
tgacaccatc gagaacgtca aagcaaagat ccaggacaag gaaggcattc ctcctgacca
                                                                       420
gcagaggttg atctttgccg gaaagcagct ggaagatggg
                                                                        460
      <210> 164
      <211> 462
      <212> DNA
      <213> Homo sapien
      <400> 164
ggcacgagcc ggatctcatt gccacgcgcc cccgacgacc gcccgacgtg cattcccgat
                                                                        60
tccttttggt tccaagtcca atatggcaac tctaaaggat cagctgattt ataatcttct
                                                                       120
aaaggaagaa cagacccccc agaataagat tacagttgtt ggggttggtg ctgttggcat
                                                                       180
ggcctgtgcc atcagtatct taatgaagga cttggcagat gaacttgctc ttgttgatgt
                                                                       240
catcgaagac aaattgaagg gagagatgat ggatctccaa catggcagcc ttitccttag
                                                                       300
aacaccaaag attgtctctg gcaaagacta taatgtaact gcaaactcca agctggtcat
                                                                       360
tatcacggct ggggcacgtc agcaagaggg agaaagccgt cttaatttgg tccagcgtaa
                                                                       420
cgtgaacatc tttaaattca tcattcctaa tgttgtaaaa ta
                                                                       462
      <210> 165
      <211> 462
```

<212> DNA



<213> Homo sapien

WO 00/37643

```
<400> 165
qqcacqagga agccatgagc agcaaagtct ctcgcgacac cctgtacgag gcggtgcggg
                                                                         60
aagteetgea egggaaceag egcaagegee gcaagtteet ggagaeggtg gagttgeaga
                                                                        120
tcagettgaa gaactatgat eeccagaagg acaagegett etegggeace gteaggetta
                                                                        180
agtocactoc cogocotaag ttototgtgt gtgtcotggg ggaccagcag cactgtgacg
                                                                        240
aggctaaggc cgtggatatc ccccacatgg acatcgaggc gctgaaaaaa ctcaacaaga
                                                                        300
                                                                        360
ataaaaaact ggtcaagaag ctggccaaga agtatgatgc gtttttggcc tcagagtctc
tgatcaagca gattccacga atcctcggcc caggtttaaa taaggcagga aagttccctt
                                                                        420
ccctgctcac acacaacgaa aacatggtgg ccaaagtgga tg
                                                                        462
      <210> 166
      <211> 459
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(459)
      \langle 223 \rangle n = A,T,C or G
      <400> 166
ggcacgagag ggacctgtnt gaatggntcc actagggttn anntgnctct tacttttaac
                                                                         60
cantnaaatn gacctgcccg tgaanangcg ggcntgacac annaanacga gaagacccta
                                                                        120
tggagettta atttattaat geanacagna eetaacaaac eeacangtee taaactacca
                                                                        180
agcctgcatt aaaaatttcg gntggggcna cctcnnagca naacccaacc tccgagcaac
                                                                        240
tcatgctaag acttcaccag tcaaagctga actactatac tcaattgatc caataacttg
                                                                        300
accaacagan caagntaccc tagggataac ancacaatcc tattctagac cccttatnac
                                                                        360
caatangntt tacacctcna tngnggaacc aggacatccg atggggcagn cgttattaaa
                                                                        420
gttngttgnt aacnataaag tctacgtgat ctgagttag
                                                                        459
      <210> 167
      <211> 464
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(464)
      \langle 223 \rangle n = A,T,C or G
      <400> 167
gaattgggac caacganaan cntgcggntc ttnttttgcn tccanngccc agctnattgc
                                                                         60
tcagacacac atggggaagg tnaaggtcgg gagtcaacng atttggtngt attgnagcgt
                                                                        120
ttggtcacca gngctgcttt taactctggn aaagtggata ttgttgtcat naatgacccc
                                                                        180
tncattgacc tnaactacat ggtttacatg ttccaatatg attccaccca tggcaaattc
                                                                        240
catngcaccg tnaaggctga gaacgggaag cttgtnatca atggaaatcc catcaccatc
                                                                        300
tttcangaac ganatccntn caaaaatcaa anttgggggc gatgcttggc cncttgaagt
                                                                        360
accettcaan gggaannncc ccactttggc cgntntttnc aancccaccc caatttgggn
                                                                        420
aaaaaaaaa gggnntttgg gggggggcct tttanntttt tttt
                                                                        464
      <210> 168
      <211> 462
```

53

<212> DNA

```
<213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(462)
       <223> n = A,T,C \text{ or } G
       <400> 168
ggcacgaggn nnaacctncg gggctggggc agcacgcctt gngcaancct gcactgcact
                                                                           60
gaagacccgg tgccggaagc cgnnggcngc nacatgcagn aactgaacca gctgggcgcg
                                                                          120
cancagttet cagacetgae agaggtgett ttacaettee taactgatee anantangtg
                                                                          180
gaaatattnt tngttnatnt catntgaatn atccancncc aatcatanca nntttnattn
                                                                          240
cctcataanc nttgagaana gennecttnt gnttneanan ggtgetntga anangagtet
                                                                          300
cacangcaan caggtecaag eggatttnnt aactntgggt ettantgang agaaagneae
                                                                          360
. ප්රයේද්ර්ර්ය ලබුවුන්ගා ඉලක් ඔහු යෙලු බහිල් ද සම්පෙත් සම්පෙත් අද අල් කරන අද අද
                                                                          420
agactetgat gattaaccag etttanatat ggaenggaaa tt
                                                                          462
      <210> 169
      <211> 460
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(460)
      <223> n = A,T,C or G
      <400> 169
ggcacgaggg acagcagacn agacagtcac agcagccttg acaaaacgtt cctggaactc
                                                                          60
aagntettnt nencaaagga ggacagagca nacagcagag accatggant etneetegge
                                                                         120
ccctccccac agatggtgca tcccctggca naggctcctg ctcacagcct cacttctaac
                                                                         180
cttctggaac ccgcccacca ctgccaagct cactattgaa tccacgccgt tcaatgnntc
                                                                         240
ntaggggaag gaggngcttt ctactnttnc acaatctgan ccccttcttn tttggttact
                                                                         300
ancatggctc theatgthaa aatactggha tgghtaacct gteaaattta tagghantht
                                                                         360
gctaattggg aaactneenn tngtetaeee caggggneee agatteetnn gtteneataa
                                                                         420
cnattaattt aacccctaat gncaanccct tngttaaaga
                                                                         460
      <210> 170
      <211> 508
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(508)
      <223> n = A, T, C or G
      <400> 170
ggcacgaggg ggatttttag gtggtcnggt gtggtatcag gaataatgtg ggaggccaga
                                                                          60
ttgaagtcca ggccaggaac aatggtaatt gtgggactta agaaagtgtg agtacagctg
                                                                         120
aatgagccgg ggagcagaaa gtatatgcgt caggtatgag gaagaaaata gattttggaa
                                                                         180
gttatgagaa atgtagagag tgagttgagc atagtttgtg attttgaggg cctctaacag
                                                                         240
tattaaagca gcggcagcgg ctgcacacag acatgatggc taggctaaaa caggaaggtc
                                                                         300
aagttgtttg gacagaaagg ctacagggtg cagtcctggc tcttgtgtaa gaattctgac
                                                                         360
cacactaacc atgcctagga aggaaaggag ttgttctttt gtaagggatt gaggtttggg
                                                                         420
```

WO 00/37643 PCT/US99/30909 55

	80
<210> 171 <211> 507 <212> DNA <213> Homo sapien	
<220> <221> misc_feature <222> (1)(507) <223> n = A,T,C or G	
<400> 171	
	60
	20 80
	40
	00
gaagaggagc atgcccttca aaaagggtgc cgcctttgag ctggtcttca tagtcctggc 3	60
	20
	80 07
	0,
<210> 172	
<211> 409	
<212> DNA <213> Homo sapien	
<400> 172	
	50
	20
	80 40
	00
	60
	09
<210> 173	
<211> 409	
<212> DNA	
<213> Homo sapien	
<400> 173	
	60
	20
	30
	40
tcagcgtctg caggatgctg aggaacatgt agaagctgtg aattccaaat gcgcttctct 30	00
	50
gtctaatgct gcctgcgctg cgcttgataa gaagcagagg aactttgac 4(9
<210> 174	
<211> 407	
<212> DNA	



<213> Homo sapien

<pre><400> 174 ggcacgagcc ggggcgggc gcggcgctcc ggctcgaggc attcggagct gcgggagccg ggctggcagg agcaggatgg cggcggcgc ggctgcaggc gaggcgcgc gggtgctggt gtacggcggc aggggcgctc tgggttctcg atgcgtgcag gcttttcggg cccgcaactg gtgggttgcc agcgttgatg tggtggagaa tgaagaggcc agcgctagca tcattgttaa aatgacagac tcgttcactg agcaggctga ccaggtgact gctgaggttg gaaagctctt gggtgaagag aaggtggatg caattctttg cgttgctga ggatgggccg ggggcaatgc caaatccaag tctctcttta agaactgtga cctgatgtgg aagcaga</pre>	60 120 180 240 300 360 407
<210> 175 <211> 407 <212> DNA <213> Homo sapien	
<pre><400> 175 ggcacgagct tgcccgtcgg tegctagctc gctcggtgcg cgtcgtcccg ctccatggcg ctcttcgtgc ggctgctggc tctcgccctg gctctggcc tgggcccgc cgcgaccctg gcgggtcccg ccaagtcgcc ctaccagctg gtgctgcagc acagcaggcc ccaacgtgtg tgctgtgcag aaggttattg gcactaatag gaagtacttc accaactgca agcagtggta ccaaaggaaa atctgtggac aatcaacagt catcagctac gagtgctgtc ctggatatga aaaggtccct ggggagaaagg gctgtccagc agccctacca ctctcaaacc tttacgagac cctgggagtc gttggatcca ccaccac</pre> <210> 176	60 120 180 240 300 360 407
<210> 176 <211> 409 <212> DNA <213> Homo sapien <400> 176	
ggcacgagtg gtgccaaaac gggaccatgc cctcctggag gagcagagca	60 120 180 240 300 360 409
<210> 177 <211> 408 <212> DNA <213> Homo sapien	
<pre><400> 177 ggcacgaggt ccaggtaact gcaaaaacaa tggctcagca tgaagaactg atgaagaaaa ctgaaacaat gaatgtagtt atggagacca ataaaatgct aagagaagag</pre>	60 120 180 240 300 360 408

<210> 178 <211> 92

```
<212> DNA
      <213> Homo sapien
      <400> 178
ggcacgagaa gaaattaaga gctaaagaca aggagaatga aaatatggtt gcaaagctga
                                                                        60
acaaaaagt taaagagcta gaagaggaga tg
                                                                         92
      <210> 179
      <211> 411
      <212> DNA
      <213> Homo sapien
      <400> 179
ggcacgagga gacacgccac ctataccaca gttctcagaa tgaattagct aagttggaat
                                                                        60
cagaacttaa gagtctcaaa gaccagttga ctgatttaag taactcttta gaaaaatgta
                                                                       120
aggaacaaaa aggaaacttg gaagggatca taaggcagca agaggctgat attcaaaatt
                                                                       180
ctaagttcag ttatgaacaa ctggagactg atcttcaggc ctccagagaa ctgaccagta
                                                                       240
ggctgcatga agaaataaat atgaaagagc aaaagattat aagcctgctt tctggcaagg
                                                                       300
aagaggcaat ccaagtagct attgctgaac tgcgtcagca acatgataaa gaaattaaag
                                                                       360
agctggaaaa cctgctgtcc caggaggaag aggagaatat tgttttagaa g
                                                                       411
      <210> 180
      <211> 411
      <212> DNA
      <213> Homo sapien
      <400> 180
ggcacgaggt tgttcggagc gggcgagcgg agttagcagg gctttactgc agagcgcgcc
                                                                        60
gggcactcca gcgaccgtgg ggatcagcgt aggtgagctg tggccttttg cgaggtgctg
                                                                       120
cagccatage tacgtgcgtt cgctacgagg attgagcgtc tccacccatc ttctgtgctt
                                                                       180
caccatctac ataatgaatc ccagtatgaa gcagaaacaa gaagaaatca aagagaatat
                                                                       240
aaagactagt totgtoccaa gaagaactot gaagatgatt cagoottotg catotggato
                                                                       300
tcttgttgga agagaaaatg agctgtccgc aggcttgtcc aaaaggaaac atcggaatga
                                                                       360
ccacttaaca tctacaactt ccagccctgg ggttattgtc ccagaatcta g
                                                                       411
      <210> 181
      <211> 411
      <212> DNA
      <213> Homo sapien
      <400> 181
ggcacgaggc gggacagggc gaagcggcct gcgcccacgg agcgcgcgac actgcccgga
                                                                        60
agggaccgcc accettgecc ceteagetge ecaetegtga tttecagegg ceteegegg
                                                                       120
cgcacgatgc cctcggccac cagccacagc gggagcggca gcaagtcgtc cggaccgcca
                                                                       180
ccgccgtcgg gttcctccgg gagtgaggcg gccgcgggag ccgggggccgc cgcgccggct
                                                                       240
teteageace eegeaacegg caceggeget gteeagaceg aggecatgaa geagattete
                                                                       300
ggggtgatcg acaagaaact tcggaacctg gagaagaaaa agggtaagct tgatgattac
                                                                       360
caggaacgaa tgaacaaagg ggaaaggctt aatcaagatc agctggatgc c
                                                                       411
      <210> 182
      <211> 411
      <212> DNA
      <213> Homo sapien
      <400> 182
```

```
ggcacgagcc gacatggagc tgttcctcgc gggccgccgg gtgctggtca ccggggcagg
                                                                          60
 caaaggtata gggcgcggca cggtccaggc gctgcacgcg acgggcgcgc gggtggtggc
                                                                         120
 tgtgagccgg actcaggcgg atcttgacag ccttgtccgc gagtgcccgg ggatagaacc
                                                                         180
 cgtgtgcgtg gacctgggtg actgggaggc caccgagcgg gcgctgggca gcgtgggccc
                                                                         240
 cgtggacctg ctggtgaaca acgccgctgt cgccctgctg cagcccttcc tggaggtcac
                                                                         300
 caaggaggcc tttgacagat cctttgaggt gaacctgcgt gcggtcatcc aggtgtcgca
                                                                        360
 gattgtggcc aggggcttaa tagcccgggg agtcccaggg gccatcgtga a
                                                                        411
       <210> 183
       <211> 409
       <212> DNA
       <213> Homo sapien
       <400> 183
 ggcacgagcc tacactctgg ccagagatac cacagtcaaa cctggagcca aaaaggacac
                                                                         60
 aaaggactct cgacccaaac tgccccagac cctctccaga ggttggggtg accaactcat
                                                                        120
 ctggactcag acatatgaag aagctctata taaatccaag acaagcaaca aacccttgat
                                                                        180
 gattattcat cacttggatg agtgcccaca cagtcaagct ttaaagaaag tgtttgctga
                                                                        240
 aaataaagaa atccagaaat tggcagagca gtttgtcctc ctcaatctgg tttatgaaac
                                                                        300
 aactgacaaa cacctttctc ctgatggcca gtatgtcccc aggattatgt ttgttgaccc
                                                                        360
 atctctgaca gttagagccg atatcactgg aagatattca aatcgtctc
                                                                        409
       <210> 184
       <211> 410
       <212> DNA
       <213> Homo sapien
       <400> 184
ggcacgaggt cattccagca ccaacaggat ccaagccaga ttgattgggc tgcattggcc
                                                                        60
caagettgga ttgcccaaag agaagettca ggacagcaaa gcatggtaga acaaccacca
ggaatgatgc caaatggaca agatatgtct acaatggaat ctggtccaaa caatcatggg
                                                                        120
                                                                       180
aatttccaag gggattcaaa cttcaacaga atgtggcaac cagaatgggg aatgcatcag
                                                                       240
caacccccac acccccctcc agatcagcca tggatgccac caacaccagg cccaatggac
                                                                       300
attgttcctc cttctgaaga cagcaacagt caggacagtg gggaatttgc ccctgacaac
                                                                       360
aggcatatat ttaaccagaa caatcacaac tttggtggac cacccgataa
                                                                       41.0
      <210> 185
      <211> 411
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(411)
      <223> n = A,T,C or G
      <400> 185
ggcacgagca cagatgtagt tttctctgcg cgtgtgcgtt ttccctcctc ccccgccctc
agggtccacg gccaccatgg cgtattaggg gcagcagtgc ctgcggcagc attggccttt
                                                                        60
                                                                       120
gcagcggcgg cagcagcacc aggctctgca gcggcaaccc ccagcggctt aagccatggc
                                                                      180
gcttctcacg gcattcagca gcagcgttgc tgtaaccgac aaagacacct tcgaattaag
                                                                      240
cacatteete gatteeagea aageaeegea acatgaeega aatgagette etgageageg
                                                                      300
aggtgttggt gggggacttg atgtccccct tcgacccgtc gggtttgggg gctgaagaaa
                                                                      360
gcctangtct cttagatgat tacctggagg tggccaagca cttcaaacct c
                                                                      411
```

120

180

```
<210> 186
      <211> 410
      <212> DNA
      <213> Homo sapien
      <400> 186
ggcacgaget tetagteceg ceatggeege teteaceegg gaceeceagt tecagaaget
                                                                        60
gcagcaatgg taccgcgagc accgctccga gctgaacctg cgccgcctct tcgatgccaa
                                                                        120
caaggaccgc ttcaaccact tcagcttgac cctcaacacc aaccatgggc atatcctggt
                                                                       180
ggattactcc aagaacctgg tgacggagga cgtgatgcgg atgctggtgg acttggccaa
                                                                       240
gtccaggggc gtggaggccg cccgggagcg gatgttcaat ggtgagaaga tcaactacac
                                                                       300
cgagggtcga gccgtgctgc acgtggctct gcggaaccgg tcaaacacac ccatcctggt
                                                                       360
agacggcaag gatgtgatgc cagaggtcaa caaggttctg gacaagatga
                                                                       410
      <210> 187
      <211> 506
      <212> DNA
      <213> Homo sapien
      <400> 187
ctttcgtggc tcactccctt tcctctgctg ccgctcggtc acgcttgtgc ccgaaggagg
                                                                        60
aaacagtgac agacctggag actgcagttc tctatccttc acacagctct ttcaccatgc
                                                                       120
ctggatcact tcctttgaat gcagaagctt gctggccaaa agatgtggga attgttgccc
                                                                       180
ttgagatcta ttttccttct caatatgttg atcaagcaga gttggaaaaa tatgatggtg
                                                                       240
tagatgctgg aaagtatacc attggcttgg gccaggccaa gatgggcttc tgcacagata
                                                                       300
gagaagatat taactctctt tgcatgactg tggttcagaa tcttatggag agaaataacc
                                                                       360
tttcctatga ttgcattggg cggctggaag ttggaacaga gacaatcatc gacaaatcaa
                                                                       420
agtetgtgaa gaetaatttg atgeagetgt ttgaagagte tgggaataea gatatagaag
                                                                       480
gaatcgacac aactaatgca tgctat
                                                                       506
      <210> 188
      <211> 506
      <212> DNA
      <213> Homo sapien
      <400> 188
gccacagagg cggcggagag atggccttca gcggttccca ggctccctac ctgagtccag
                                                                        60
ctgtcccctt ttctgggact attcaaggag gtctccagga cggacttcag atcactgtca
                                                                       120
atgggaccgt tctcagctcc agtggaacca ggtttgctgt gaactttcag actggcttca
                                                                       180
gtggaaatga cattgccttc cacttcaacc ctcggtttga agatggaggg tacgtggtgt
                                                                       240
gcaacacgag gcagaacgga agctgggggc ccgaggagag gaagacacac atgcctttcc
                                                                       300
agaaggggat gccctttgac ctctgcttcc tggtgcagag ctcagatttc aaggtgatgg
                                                                       360
tgaacgggat cctcttcgtg cagtacttcc accgcgtgcc cttccaccgt gtggacacca
                                                                       420
tctccgtcaa tggctctgtg cagctgtcct acatcagctt ccagcctccc ggcgtgtggc
                                                                       480
ctgccaaccc ggctcccatt acccag
                                                                       506
      <210> 189
      <211> 399
      <212> DNA
      <213> Homo sapien
      <400> 189
ctggacagga gaagagcctg gctgctgaag gcagggctga cacgaccacg ggcagcattg
                                                                        60
```

ctggagcccc agaggatgaa agatcgcaga gcacagcccc ccaggcacca gagtgcttcg

accetgeegg aceggetggg etegtgagge egacatetgg cettteecag ggeecaggaa

aggaaacctt ggaaagtgct ctaatcgctc tagactctga aaaacccaag aaacttcgct tccacccaaa gcagctgtac ttctctgcca ggcagggtga gctgcagaag gtgcttctca tgctggttga tggaattgat cccaacttca aaatggagca ccaaagtaag cgttccccat tacatgctgc tgcggaggct ggccacgtgg acatctgcc	240 300 360 399
<210> 190 <211> 401 <212> DNA <213> Homo sapien	
<400> 190 cggcgacggt ggtggtgact gagcggagcc cggtgacagg atgttggtgt tggtattagg agatctgcac atcccacacc ggtgcaacag tttgccagct aaattcaaaa aactcctggt	60
gccaggaaaa attcagcaca ttotctgcac aggaaacctt tgcaccaaag agagttatga ctatctcaag actctggctg gtgatgttca tattgtgaga ggagacttcg atgagaacct	120 180 240 :
gaallaleea gaacagaaag tigigacigi iggacagiic aaaaiiggic igaiccaigg	300
acatcaagtt attocatggg gagatatggc cagcttagcc ctgttgcaga ggcaatttga tgtggacatt cttatctcgg gacacacaca caaatttgaa g	360. 401
<210> 191	
<211> 406 <212> DNA	
<213> Homo sapien	
<400> 191	
tggcagccta agccgtggga gggttccagt cgagaatggg aagatgaaag acttcagatg gaacagaaat aaatgccttt tttgacaaac gcagcagtgc gtgcctctag cttgcaagag	60
cgttactcc cttcatagct ttaaaaggtt ttcgcactgc gtgcagttag agtagctaaa	120 180
terrigigiga egeteeacaa acaettgiaa gaattitigea gagaaagata accettgeea	240
cocaatgood cocacaggoa tictactood cagtacotot tagggtggga gaaatggfga	300
agagttgttc ctacaacttg ctaacctagt ggacagggta gtagattagc atcatccgga tagatgtgaa gaggacggct gtttggataa taattaagga taaaat	360
<210> 192	406
<210> 192	
<212> DNA	
<213> Homo sapien	
<400> 192	
cccggggagg ccctggtcat aaaactttaa attttactag tgttacttaa tgtatattct	. 60
aaaaagagaa tgcagtaact aatgccctaa atgtttgatc tctgtttgtc attacttttt caaaattatt tttttctgta aagtataata tataaaaactt cttgcttaaa ttgaatttct	120
atattagtgg ttaattgcag tttattaaag ggatcattat cagtaatttc atagcaactg	180
ttetagtgtt tigigititt aaaacagaat taggaatitg agatatetga ttatarrirr	240 300
catatgaatc acagac	316
<210> 193	
<211> 146	
<212> DNA <213> Homo sapien	
<400> 193 qaaacatgga ctgccctta aattttgagt gtggtaaaaa gatattaa gatatt	
gaaacatgga ctgcccctta aattttgact gtcctaaaaa cctatttctg atttataata tgctgcctga taaagtgaca ctagatgtac cagctgagtg tttaatcttc ccatcacaga	60
tcagatttga gcattaacag gtattt	120 146

```
<210> 194
      <211> 405
      <212> DNA
      <213> Homo sapien
      <400> 194
                                                                        60
cggatgtgct cactgacatt ctactccaag tcggagatgc agatccactc caagtcacac
accgagacca agccccacaa gtgcccacat tgctccaaga ccttcgccaa cagctcctac
                                                                       120
                                                                       180
ctggcccagc acatccgtat acactcaggg gctaagccct acagttgtaa cttctgtgag
                                                                       240
aaatccttcc gccagctctc ccaccttcag cagcacaccc gaatccacac tggtgataga
ccatacaaat gtgcacaccc aggctgtgag aaagccttca cacaactctc caatctgcag
                                                                       300
teccacagae ggeaacacaa caaagataaa eeetteaagt geeacaaetg teategggeg
                                                                       360
                                                                       405
tacacggatg cagecteact agaggtgeac etgtetacge acaca
      <210> 195
      <211> 421
      <212> DNA
      <213> Homo sapien
      <400> 195
agaattegge aegagetaet eettgegege tggeaeteeg eageetttaa ggttegegeg
                                                                        60
ggggccaggc aagagttagc catgaagagc ctcaagtccc gcctgaggag gcaggacgtg
                                                                       120
                                                                       1.80
cccggccccg cgtcgtctgg cgccgccgcc gccagcgcgc atgcagcaga ttggaataaa
                                                                       240
tatgatgacc gattgatgaa agcagcagaa aggggggatg tagaaaaagt gacgtcaatc
cttgctaaaa agggggtcaa tccaggcaaa ctagatytgg aaggcagatc tgtcttccat
                                                                       300
gttgtgacct caaaggggaa tcttgagtgt ttgaatgcca tccttataca tggagttgat
                                                                       360
                                                                       420
attacaacca gtgacactgc agggagaaat gctcttcacc tggctgctaa gtatggacat
                                                                       421
g
      <210> 196
      <211> 476
      <212> DNA
      <213> Homo sapien
      <400> 196
                                                                        60
agaattgatc tatagattta atgcaatgcc tactaaaatc ccagtacgat tttttacagg
catagacaat agacatagcc aaaacttatt ctaaaataca tatgaagatg cacaggccct
                                                                       120
                                                                       180
aqttatacaa tcttqacaaa gaagaataaa gtgggaagaa tctatttgat tttaaggctt
                                                                       240
accatgtaac tacagtcatc aagagagtgt ggtatcggca gacggtcaga catacagatc
                                                                       300
aatggaatgt aacagaggac ccagaaatag gcccacacag atatgctcaa tggatatttg
acaagcgtgc aaaacaattc aatggaagaa taagctttca aaaaaatggc gttggagcaa
                                                                       360
ccggacatcc ataggaaaaa atgaacccat acctaaacca taaaccttat ataaaaataa
                                                                       420
                                                                       476
acacaaaatg aatcataggc ttaaatgtaa gctataaaac ttttagagaa aaacac
      <210> 197
      <211> 503
      <212> DNA
      <213> Homo sapien
      <400> 197
                                                                        60
tagccctcgg tgaagcccca gaccacagct atgagtccct tcgtgtgacg tctgcgcaga
                                                                       120
aacatgttct gcatgtccag ctcaaccggc ccaacaagag gaatgccatg aacaaggtct
                                                                       180
tctggagaga gatggtagag tgcttcaaca agatttcgag agacgctgac tgtcgggcgg
tgqtqatctc tggtgcagga aaaatgttca ctgcaggtat tgacctgatg gacatggctt
                                                                       240
```

300

360

420

480

503

```
cggacatcct gcagcccaaa ggagatgatg tggcccggat cagctggtac ctccgtgaca
tcatcactcg ataccaggag accttcaacg tcatcgagag gtgccccaag cccgtgattg
ctgccgtcca tgggggctgc attggcggag gtgtggacct tgtcaccgcc tgtgacatcc
ggtactgtgc ccaggatgct ttcttccagg tgaaggaggt ggacgtgggt ttggctgccc
atgtaggaac actgcagcgc ctq
      <210> 198
      <211> 168
      <212> PRT
      <213> Homo sapien
      <400> 198
Phe Val Ala His Ser Leu Ser Ser Ala Ala Ala Arg Ser Arg Leu Cys
                 5
                                     10
Pro Lys Glu Glu Thr Val Thr Asp Leu Glu Thr Ala Val Leu Tyr Pro
                                 25
Ser His Ser Ser Phe Thr Met Pro Gly Ser Leu Pro Leu Asn Ala Glu
                             40
Ala Cys Trp Pro Lys Asp Val Gly Ile Val Ala Leu Glu Ile Tyr Phe
                         55
Pro Ser Gln Tyr Val Asp Gln Ala Glu Leu Glu Lys Tyr Asp Gly Val
                    70
                                       ..75
Asp Ala Gly Lys Tyr Thr Ile Gly Leu Gly Gln Ala Lys Met Gly Phe
                85
                                    90
Cys Thr Asp Arg Glu Asp Ile Asn Ser Leu Cys Met Thr Val Val Gln
                                105
Asn Leu Met Glu Arg Asn Asn Leu Ser Tyr Asp Cys Ile Gly Arg Leu
                            120
Glu Val Gly Thr Glu Thr Ile Ile Asp Lys Ser Lys Ser Val Lys Thr
                        135
                                            140
Asn Leu Met Gln Leu Phe Glu Glu Ser Gly Asn Thr Asp Ile Glu Gly
                    150
                                        155
Ile Asp Thr Thr Asn Ala Cys Tyr
                165
      <210> 199
      <211> 168
      <212> PRT
   <213> Homo sapien
      <400> 199
His Arg Gly Gly Glu Met Ala Phe Ser Gly Ser Gln Ala Pro Tyr
                                    10
Leu Ser Pro Ala Val Pro Phe Ser Gly Thr Ile Gln Gly Gly Leu Gln
Asp Gly Leu Gln Ile Thr Val Asn Gly Thr Val Leu Ser Ser Gly
                            40
Thr Arg Phe Ala Val Asn Phe Gln Thr Gly Phe Ser Gly Asn Asp Ile
                        55
                                            60
Ala Phe His Phe Asn Pro Arg Phe Glu Asp Gly Gly Tyr Val Val Cys
                    70
                                        75
Asn Thr Arg Gln Asn Gly Ser Trp Gly Pro Glu Glu Arg Lys Thr His
                                    90
Met Pro Phe Gln Lys Gly Met Pro Phe Asp Leu Cys Phe Leu Val Gln
```

105

110

100

 Ser
 Asp
 Phe
 Lys
 Val
 Met
 Val
 Asn
 Gly
 Ile
 Leu
 Phe
 Val
 Gln
 Tyr

 Phe
 His
 Arg
 Val
 Asp
 Thr
 Ile
 Ser
 Val
 Asn
 Gly

 130
 135
 140
 140

 Ser
 Val
 Gln
 Leu
 Ser
 Tyr
 Ile
 Ser
 Phe
 Gln
 Pro
 Pro
 Gly
 Val
 Trp
 Pro

 145
 150
 150
 155
 160
 160

 Ala
 Asn
 Pro
 Ala
 Pro
 Ile
 Thr
 Gln

63

<210> 200

WO 00/37643

<211> 132

<212> PRT

<213> Homo sapien

<400> 200

Val Asp Ile Cys 130

<210> 201

<211> 120

<212> PRT

<213> Homo sapien

<400> 201

 Met
 Leu
 Val
 Leu
 Gly
 Asp
 Leu
 His
 Ile
 Pro
 His
 Arg
 Cys
 Asn

 Ser
 Leu
 Pro
 Ala
 Lys
 Phe
 Lys
 Lys
 Leu
 Leu
 Val
 Pro
 Gly
 Lys
 Ile
 Gln

 His
 Ile
 Leu
 Cys
 Thr
 Gly
 Asn
 Leu
 Cys
 Thr
 Lys
 Gly
 Asp
 Tyr

 Leu
 Lys
 Thr
 Leu
 Ala
 Gly
 Asp
 Val
 His
 Ile
 Val
 Arg
 Gly
 Asp
 Phe
 Asp

 Glu
 Asn
 Leu
 Asn
 Tyr
 Pro
 Glu
 Gln
 Lys
 Val
 Val
 Thr
 Val
 Gly
 Asp
 Met

 Glu
 Asn
 Leu
 Ile
 His
 Gly
 His
 Gln
 Val
 Val
 Thr
 Val
 Gly
 Asp
 Met

 <t

```
115
                             120
       <210> 202
       <211> 135
       <212> PRT
       <213> Homo sapien
      <400> 202
Arg Met Cys Ser Leu Thr Phe Tyr Ser Lys Ser Glu Met Gln Ile His
Ser Lys Ser His Thr Glu Thr Lys Pro His Lys Cys Pro His Cys Ser
Lys Thr Phe Ala Asn Ser Ser Tyr Leu Ala Gln His Ile Arg Ile His
ser Gly Ala Lys Pro Tyr Ser Cys Asn Phe Cys Glu Lys ser Phe Arg
                        55
Gln Leu Ser His Leu Gln Gln His Thr Arg Ile His Thr Gly Asp Arg
                                        75
Pro Tyr Lys Cys Ala His Pro Gly Cys Glu Lys Ala Phe Thr Gln Leu
                85
                                    90
Ser Asn Leu Gln Ser His Arg Arg Gln His Asn Lys Asp Lys Pro Phe
                                105
Lys Cys His Asn Cys His Arg Ala Tyr Thr Asp Ala Ala Ser Leu Glu
                            120
Val His Leu Ser Thr His Thr
    130
      <210> 203
      <211> 135
      <212> PRT
      <213> Homo sapien
      <400> 203
Leu Leu Leu Ala Arg Trp His Ser Ala Ala Phe Lys Val Arg Ala Gly
Ala Arg Gln Glu Leu Ala Met Lys Ser Leu Lys Ser Arg Leu Arg Arg
                                25
Gln Asp Val Pro Gly Pro Ala Ser Ser Gly Ala Ala Ala Ser Ala
His Ala Ala Asp Trp Asn Lys Tyr Asp Asp Arg Leu Met Lys Ala Ala
Glu Arg Gly Asp Val Glu Lys Val Thr Ser Ile Leu Ala Lys Lys Gly
Val Asn Pro Gly Lys Leu Asp Val Glu Gly Arg Ser Val Phe His Val
                85
                                    90
Val Thr Ser Lys Gly Asn Leu Glu Cys Leu Asn Ala Ile Leu Ile His
                                105
Gly Val Asp Ile Thr Thr Ser Asp Thr Ala Gly Arg Asn Ala Leu His
                           120
Leu Ala Ala Lys Tyr Gly His
    130
                        135
```

<210> 204

<211> 167

<212> PRT

60

120

180

240

300

360

381



<213> Homo sapien

<400> 204 Ala Leu Gly Glu Ala Pro Asp His Ser Tyr Glu Ser Leu Arg Val Thr 10 Ser Ala Gln Lys His Val Leu His Val Gln Leu Asn Arg Pro Asn Lys 25 Arg Asn Ala Met Asn Lys Val Phe Trp Arg Glu Met Val Glu Cys Phe 40 Asn Lys Ile Ser Arg Asp Ala Asp Cys Arg Ala Val Ile Ser Gly 60 Ala Gly Lys Met Phe Thr Ala Gly Ile Asp Leu Met Asp Met Ala Ser 70 75 Asp Ile Leu Gln Pro Lys Gly Asp Asp Val Ala Arg Ile Ser Trp Tyr 90 Leu Arg Asp Ile Ile Thr Arg Tyr Gln Glu Thr Phe Asn Val Ile Glu 100 105 Arg Cys Pro Lys Pro Val Ile Ala Ala Val His Gly Gly Cys Ile Gly 120 Gly Gly Val Asp Leu Val Thr Ala Cys Asp Ile Arg Tyr Cys Ala Gln 135 140 Asp Ala Phe Phe Gln Val Lys Glu Val Asp Val Gly Leu Ala Ala His 150 155 Val Gly Thr Leu Gln Arg Leu 165 <210> 205 <211> 381 <212> DNA <213> Homo sapien <400> 205 aaatttggga tcatcgcctg ttctgaaaac tagatgcacc aaccgtatca ttatttgttt gaggaaaaaa agaaatctgc attttaattc atgttggtca aagtcgaatt actatctatt tatcttatat cgtagatctg ataaccctat ctaaaagaaa gtcacacgct aaatgtattc ttacatagtg cttgtatcgt tgcatttgtt ttaatttgtg gaaaagtatt gtatctaact tgtattactt tggtagtttc atctttatgt attattgata tttgtaattt tctcaactat aacaatgtag ttacgctaca acttgcctaa aacattcaaa cttgttttct tttttctgtt gttttctttg ttaattcatt t

65

<210> 206

<211> 514

<212> DNA

<213> Homo sapien

<400> 206

aaaagtaaat tgcataaaat tacatccaat ttctttctct aaaccaacat attcttcacc 60 ttcacaaagc aaacacatgg tgcactgaaa ccgaggtgtt accagcttta catactgttc 120 tgccatttgt ggggggtgca accacaacat aagtcagaaa aaaagctatc cagcttttcq 180 tggaatctgg tgaagtttac acttagcgat aagcctctaa gcctgaactt agcagggcta 240 gcaaaacttt atttatttcc taactcctat tattttagaa tggttttcaa aataatactg 300 caagttccta attgaaatac aaaacagaac aaaaagctgt gagaaatctt tttttttctt 360 tggctcctta aagacttgga ataatttata ttagtgttgc atacatttta ccttctacat 420 tttgatgtac ttgctcttga aagcactaga acaaattaat tgaaataaaa cctctctgaa 480 accatttgaa tctttgatcc taccatagag tttt 514

```
<210> 207
      <211> 522
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(522)
      <223> n = A, T, C or G
      <400> 207
caagettttg gtgcatagea geengeetgg aageattetg agtgetetgt etgeeetggt
                                                                      60
gggtttcatt atcctgtctg tcaaacaggc caccttaaat cctgcctcac tgcagtgtga
                                                                     120
gittggaraaa aaraararar caacaagaag ttatgtttct tacttttatc atgattcact
                                                                     180
ttataccacg gactgetata cagecaaage cagtetgget ggaactetet etetgatget
                                                                     240
gatttgcact ctgctggaat tctgcctagc tgtgctcact gctgtgctgc ggtggaaaca
                                                                     300
ggettactet gaetteeetg ggagtgtact ttteetgeet caeagttaca ttggtaatte
                                                                     360
tggcatgtcc tcaaaaatga ctcatgactg tggatatgaa gaactattga cttcttaaga
                                                                     420
aaaaagggag aaatattaat cagaaagttg attcttatga taatatggaa aagttaacca
                                                                     480
ttatagaaaa gcaaagcttg agtttcctaa atgtaagctt tt
                                                                     522
      <210> 208
      <211> 278
      <212> DNA
      <213> Homo sapien
      <400> 208
aaaatgcact accccttttt tccaacacgg agcttaaaac aaattaatga aagagtggaa
                                                                      60
120
ataggtagat agettteact gatgtagatg tggaataaat tattactrea ggaaaaaaat
                                                                     180
tcccaaacat cttatgaaaa agtatacaac tctacttcaa aatatgctat ttactcactg
                                                                     240
ccaaagacag ttttatttga aatcttgttt ctgtattt
                                                                     278
      <210> 209
      <211> 234
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(234)
      <223> n = A, T, C or G
      <400> 209
cctcccaaat ttagcaggtg ctgggnagga ccctagggag tggtttatgg gggctagctg
                                                                     60
gtgaaactgc cctttccttt ctgttctatg agtgtgatgg tgtttgagaa aatgtggggc
                                                                    120
tatggttcag gcgcacttca catgtgcaaa gatggagaaa gcactcacct acacgtttag
                                                                    180
gctcagaatg ttgattgaaa cattttgaat gatcaaaaat aaaatgttat tttt
                                                                    234
     <210> 210
     <211> 186
     <212> DNA
     <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1)...(186)
      <223> n = A,T,C or G
      <400> 210
aaaataactg atggcaaaat aaaanattta catcacatca tactgtgtaa acatgtaagg
                                                                         60
tctctgtaca aagaaatata catgcaaaat aatgtaaaaa tttaactgaa ataataaaag
                                                                        120
aaacaataca caaataaaaa ttatgaggtt acgaatacac atccagtttc gaatccaatt
                                                                        180
tctttt
                                                                        186
      <210> 211
      <211> 403
      <212> DNA
      <213> Homo sapien
      <400> 211
aaaaattggt aaaatattta agtacaaaat aagtagcttc cagcgaggtt tttataccat
                                                                        60
agtaagagca cacaatagat attactagca cacatgggtt atctgggagc gctatagcta
                                                                       120
caataaacct aattatggaa cagaaatttg cattctgttt ccagtgctac tacactccta
                                                                       180
ctttctcaaa agtctgctct attaatatca gctcagtgca gtttactatg aatagtttat
                                                                       240
gtctgtgatg caaagcatta attgttctct ttttacaaac atacatttt ttcataagga
                                                                       300
agactggggg aaaacccaga aacatacaga gaaaaggaaa gcatcatcaa atatatgtta
                                                                       360
aaaattaaga tgatgtttac tactagtcat cctacaacaa ttt
                                                                       403
      <210> 212
      <211> 345
      <212> DNA
      <213> Homo sapien
      <400> 212
cctctttatg agttcattac tgctgttcag tctcggcaca cagacacccc tgtgcaccgg
                                                                        60
ggtgtacttt ctactctgat cgctgggcct gtggttgaga taagtcacca gctacggaag
                                                                       120
gtttctgacg tagaagagct tacccctcca gagcatcttt ctgatcttcc accattttca
                                                                       180
aggtgtttaa taggaataat aataaagtct tcgaatgtgg tcaggtcatt tttggatgaa
                                                                       240
ttaaaggcat gtgtggcttc taatgatatt gaaggcattg tgtgcctcac ggctgctgtg
                                                                       300
catattatcc tggttattaa tgcaggtaaa cataaaagct caaaa
                                                                       345.
      <210> 213
      <211> 318
      <212> DNA
      <213> Homo sapien
      <400> 213
aaaatgtttt attattttga aaataatgtt gtaattcatg ccagggactg acaaaagact
                                                                        60
tgagacagga tggttattct tgtcagctaa ggtcacattg tgcctttttg acctttctt
                                                                       120
cctggactat tgaaatcaag cttattggat taagtgatat ttctatagcg attgaaaggg
                                                                       180
caatagttaa agtaatgagc atgatgagag tttctgttaa tcatgtatta aaactgattt
                                                                       240
ttagctttac aaatatgtca gtttgcagtt atgcagaatc caaagtaaat gtcctgctag
                                                                       300
ctagttaagg attgtttt
                                                                       318
      <210> 214
      <211> 462
      <212> DNA
      <213> Homo sapien
```

```
<400> 214
aaacacatct ggttctggca gcaagttata ttatgcattt agagcaatag gtgccctgaa
                                                                        60
agttattgtt gctttttttg ttttttttt cagtttgtgc gtgtcacttg aatcagaaac
                                                                       120
caaacacatg taaaaaaata tcatcctcaa tgccccccat taactctctc tccagaaggt
                                                                       180
gacaatgtta gtgaactcaa gactctcact gatgatggta ttttacaatg aaaacacaag
                                                                       240
gaaacccttt gaggtccaat tttcacatca tattctccaa atagtaaaat agcagctcta
                                                                       300
catgitgatg aaaagaaatt tcaatttctt cctatttgtt tttactcata tcaacattaa
                                                                       360
tatgtatctg gatttattaa tttccaaaaa gaaaatttta gttaccaaat atttcagaaa
                                                                       420
tttaataaag cattatatat atgtaattag cacttatcta cc
                                                                       462
      <210> 215
      <211> 280
      <212> DNA
      <213> Homo sapien
      <400> 215
aaacttttct gaaacgatta gctgtagcca aattatgtgg ttacgttttg ctacattaga.
                                                                        60
atttgaaaat gcaatatgtg tggtaaatct actgtttgaa atttataatg gtctctgata
                                                                       120
tgattcgaat tttggtaact tttgaaagtt attttccccc tttagtcatg gatttctatt
                                                                       1.80
tgttttttaa tgttaatttt tctagaaagc atctgaattg actaggcttt tcctatataa
                                                                       240.
aaaactcaaa acttgttaac tctgtacttt aataaaattt
                                                                       28:0
      <210> 216
      <211> 210
      <212> DNA
      <213> Homo sapien
      <400> 216
aaaatctctg gcttcaaagt ttcttgggga aaggtcggtt tacctcacat tttttgtttc
                                                                        60
cattagtaat attctaggta cctcacaaaa tgtattatgg tgccatggct gttagttttt
                                                                       120
agtgagtgct gtaggattaa ttcgaaaata ggcagaattc cattcctccc aaggtggcaa
                                                                       180
aaattagcta tactgatgta attgtcattt
                                                                       210
      <210> 217
      <211> 398
      <212> DNA
      <213> Homo sapien
      <400> 217
ctggagctgc tagaacttga gatgagggca agagcgatta aagccctaat gaaagctggt
                                                                        60
gatataaaaa agccagccta ggtatttaac ttgattttga attttaggta tgtttgaaca
                                                                       120
aagccacatc atttaatttt gtatctaaaa tttatttggg gtcttatatg ttatttctca
                                                                       180
tgtaaccctt attaggactc attttagccc taaattacct gtggctgttt ctttttattt
                                                                       240
ttttgactac ttttatatta taaatgtgtg ttactgtctt atgaattcat ggcaatatag
                                                                       300
ttggatagcc tggatacttt gttagatgag tatttagctg tgtctgcaaa tcttaaaagc
                                                                       360
cattagcaaa gagtcgtggt atttttttt ttattttt
                                                                       398
      <210> 218
      <211> 487
      <212> DNA
      <213> Homo sapien
      <400> 218
ctgccgccgg tcaggctggt taaagatcag gtcccccagg accttgcgat ttatgtcgcc
                                                                        60
```

```
attctccagc aagacctcag tgccgaagac ctctacgatg cgccggtggg cagggtatcc
                                                                       120
tggctgcacg acgtgccggg ccatcacgtc cacgtcaatc accgcacagc ccagtttcag
                                                                       180
tqtttttaca cattatattg ttataatctc acaataacta taaattaggt agaacaggaa
                                                                       240
atgaggtttg gagaagatac ttgacttatc cgaccatctg tacttgtccc atagtaagga
                                                                       300
gcctcaagca gagacaaagg aggaagttgc ctatgttgta tggtttacag gccataaatg
                                                                       360
aatgtcatct ttttcctccc ctggggaaaa atgtctcaaa aatcccacca taggacatga
                                                                       420
catctccaga acctctatta caaaatacac atttcctgta gaggggtaac aaatttgggt
                                                                       480
                                                                       487
taacctg
      <210> 219
      <211> 390
      <212> DNA
      <213> Homo sapien
      <400> 219
aaaaaataca ccacacgata caactcaata caggagtatt tettetcaaa ttettetage
accatcaaca ttcttcaagt atctgaaata ctattaatta gcacctttgt attatgaaca
                                                                       120
aaacaaaaca aggacctcag ttcatctctg tctaggtcag cacctaacaa tgtggatcac
                                                                       180
actcatggga aagtgttttg aggtagttta aacctttgga agtttgggtt ttaaacttcc
                                                                       240
ctctgtggaa gatattcaaa agccacaagt ggtgcaaatg tttatggttt ttattttca
                                                                       300
attittatit tggttttctt acaaaggttg acattitcca taacaggtgt aagagtgttg
                                                                      . 360
aaaaaaaagt tcaaattttt gggggagcgg
                                                                       390
      <210> 220
      <211> 341
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (341)
      <223> n = A, T, C or G
      <400> 220
aaaacaggca aagttttaca gagaggatac atttaataaa actgcgagga catcaaagtg
                                                                        60
gtaaatactg tgaaatacct tttctnnnca aaaggcaaat attgaagttg tttatcaact
                                                                       120
tcgctagaaa aaaaaaaaca cttggcatac aaaatattta agtgaaggag aagtctaacg
                                                                       180
ctgaactnnn aatgaaggga aattgtttat gtgttatgaa catccaagtc tttcttcttt
                                                                       240
tttaagttgt caaagaagct tccacaaaat tagaaaggac aacagttctg agctgtaatt
                                                                       300
tcgccttaaa ctctggacac tctatatgta gtgcattttt a
                                                                       341
      <210> 221
      <211> 234
      <212> DNA
      <213> Homo sapien
      <400> 221
ccagggggaa ttgagggagg ctctaagcta ggggcactgc atggtgggac aggatggccc
                                                                        60
cttqaqqact qaaccctggg gagaagacaa acagtaataa taaaaacaaa taacaagtac
                                                                       120
tttaagaatg gattgtatga cctatagtga cagatgacat cactaatact gaaagcttct
                                                                       180
tatattaata attttggcaa aatgtcattt tgtaatatag tatatgcttt ccag
                                                                       234
      <210> 222
      <211> 186
```

<212> DNA

```
<213> Homo sapien
       <400> 222
 aaattttcat tgagttgtcc atctccagca tatagggctt caggagcaga gcagaccttg
                                                                        60
 tttttagtgg ttccatggga taaaatggga ttggaggagc tagaagaatt cagggtctgg
                                                                        120
 tccaatctgc cagtcttcct gaaatatcga aaatacacca gggctgctat atcagagcca
                                                                        180
 ccctgg
                                                                        186
       <210> 223
       <211> 486
       <212> DNA
       <213> Homo sapien
       <400> 223
ccataagcag ataagtagca gttcaactgg atgtctctct tctccaaatg ctacagtaca
                                                                        60 ·
aagccctaag catgagtgga aaatcgttgc ttcagaaaag acttcaaata acacttactt
                                                                       120
gtgcctggct gtgctggatg gtatattctg tgtcattttt cttcatggga gaaacagccc
                                                                       180
acagagetea ceaacaagta etecaaaaet aagtaagagt ttaagetttg agatgeaaca
                                                                       240
agatgageta ategaaaage ceatgtetee tatgeagtae geacgatetg gtetgggaae
                                                                       300
agcagagatg aatggcaaac.tcatagctgc.aggtggctat aacagagagg aatgtcttcg
                                                                       360
aacagtcgaa tgctataatc cacatacaga tcactggtcc tttcttgctc ccatgagaac
                                                                       420
accaagagce egatttcaaa tggctgtact catgggecag etetatgtgg taggtggate
                                                                       480
aaatgg
                                                                       486
      <210> 224
      <211> 322
      <212> DNA
      <213> Homo sapien
      <400> 224
aaatgttcac tatgtcattt agtgtccaac tttacggata ggttgactat ctaaataggc
                                                                        60
atttttagtc attaaaaaaa aatctagtca ccaggaggat ccctataact caaaataact
                                                                       120
tgtttgtaaa agaaaatttg tttacttacc cattagtaag ttcctgcata ttcattataa
                                                                       180
gatggcaaat caaacttttc taggatgaag acagcttatt tttaagttgt atagtcttag
                                                                       240
ttggtttagg gtctcaattt taattaataa aatacttggt ttttatttgc ttgtcctttt
                                                                       300
gaattcctgt tttaataatt tt
                                                                       322
      <210> 225
      <211> 489
      <212> DNA
      <213> Homo sapien
      <400> 225
aaatgtagga ataaaatggc tggcatctaa gcactttagt aaaagaggtt tttacaaata
                                                                       60
actaaggatt gtagagette ettetettt tttteettt tetteettt gttttacatg
                                                                      120
aactcaactt attcctaaca tttgtctacc tcaaagaaat ttcaagatta tttagataac
                                                                      180
atggatatgt gccaaatcct ttgagctgtt aagatgataa tttcctgctt tcctcctaca
                                                                      240
tetteteete ceaeteeete etttggtgtg aatattgget teecaattaa gaeettttt
                                                                      300
tttttttcc agtttgtttt agcttattat aggttttgga ggaactttgc cattttgtaa
                                                                      360
tettteaaat cattetteac eetteeteac ateagettee tgetttteec agtgttttae
                                                                      420
tgtaaattgt gtagcatatg acaaatcttg agctgacttt cctcttcact gatgtcatct
                                                                      480
tgagctctt
                                                                      489
```

<210> 226 <211> 398

```
<212> DNA
      <213> Homo sapien
      <400> 226
caagggccca ccgcagagca cacctatgct atggggagcc ctgctggcag ccccgagagc
                                                                        60
catgccatgg cctgcaggag ccaggctcct gtgtggatga agtccctctt cctctgtgcc
                                                                       120
ttgatccctt gggggtgcct ttggtcatct cttctgtcct ttcctgtctc tgaaatagtc
                                                                       180 .
atcactcccc ttgactctct ctgttcacgt cttctcagtc tgcagagtta acttctgtaa
                                                                       240
ggagtttaat ctggggttcc aagaaaacaa gttccttgtt aacatagcac tgactttgca
                                                                       300
acaatagaaa actaacaaat gagcaacaat ataaagagta gaggtagttc tcattgggtg
                                                                       360
taacttcaac ccattctgct tgtggttaga atttataa
                                                                      : 398
      <210> 227
      <211> 535
      <212> DNA
      <213> Homo sapien
      <400> 227
ctgctgcata gaaaatatgc taacatacaa cagtcaagtt taagcctgtg catagagaag
                                                                        60
ataaagcact tatggtaact gcaaatggta acgagtcctt aaggtttgta caacctagta
                                                                       120
tgggtccata aggaaaaact gtagtagaaa tggttaggac aaacaataaa gtagaaacag
                                                                       180
gggggaaact tgagaagaga agaaagaagc aagaaaaaaa gactttcaat tgtataaaat
                                                                       240 .
tcacaaacca gtaaagtata aagacaccat ggagaaatgg ttaactctgc cccaaacacc
                                                                       300
caacagcaaa caaaaccaga atgaataago otttggcaga caattttaga aatttgaatg.
                                                                       360
ttacatttct caataattca caaacaatat attatatggt atatttatat taaatattgg
                                                                       420
gaaaccaatg ttgtaaattt gatgettata atgetttage caatgagage acaatgatat
                                                                       480
caatcaaget aaatgaatge tggtgttate acaacagtge teatttatga aacaa
                                                                       535
      <210> 228
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 228
aaacaataaa caccatcaac cttartgact ttattgtccc traaattata ttgactgttg
                                                                        60
tgattccatc aagtitgtac actcttttct ctccctgttt tgcagcaaca aattgcgaag
                                                                       120
tgcttttgtt tgtttgtttt cgtttggtta aagettattg ccatgctggt gcggctatgg
                                                                       180
agactgtctg gaaggcttgg aatggtttat tgcttatggt aaaatttgcc tgatttctta
                                                                       240
caggcagcgt ttggaaacct tttattatat agttgtttac atacttataa gtctatcatt
                                                                       300
                                                                       301
      <210> 229
      <211> 420
      <212> DNA
      <213> Homo sapien
      <400> 229
aaagttgctt tgctggaagt ttttataagg aatctcagat taaaccttta gaagtttaat
                                                                       60
tgacactagg aagccaaacc aaggctgact tcagactttg tttgtagtac ctgtgggttt
                                                                       120^
attacctatg ggtttatatc ctcaaatacg acattctagt caaagtcttg gtaatataac
                                                                       180
caatgttttc aaatgtattc tgtcatacaa agagcagatt tttattgaac ttgtgcaata
                                                                      240
actatattac catacaatat aaatattcat gaatagtttc ccaagtctgg agcgaccaca
                                                                      300
tagggagaaa atgcaaatgt ctcaattttt gttcacaaaa gtatatttta tcaaattgct
                                                                      360
gtaagctgtg gatagcttaa aagaaaaaaa gtttcctgaa atctgggaaa caagacattt
                                                                      420
```

```
<210> 230
       <211> 419
       <212> DNA
       <213> Homo sapien
       <400> 230
gtgaagtcct aaagcttgca ttccaccagc ttctacaata gccggcttat tactagagca
                                                                         60
gacagatage acetteagea etetgettgt ggtecacagt agtttttegt aagtataggt
                                                                        120
cctcattata tttactaaag cttggggtcc accactagcc agtatgatga gcttgctttc
                                                                        180
ttggttgcca taagctaaaa tttgaaggca gtctgtcgta atagccaaga atttaacatt
                                                                        240
tgttttgttg agcaaggcaa ccattttctg cagcccacca gctaaacgca ctgccatttt
                                                                        300
agctccttct tgatgtaata aaaggttgtg gagagttgta atggcataaa acaacacaga
                                                                        360
atccactggt gaaccaagca tittcaccag ggcaggaatg cctccagact taaagatgg
                                                                        419
       <210> 231
       <211> 389
       <212> DNA
       <213> Homo sapien
       <400> 231
ttgttcagag ccctggtgga tcttgcaatc cagtgcccta caaaggctag aacactacag
                                                                        60
gggatgaatt cttcaaatag gagccgatgg atctgtggtc ctttgggact catcaaagcc
                                                                        120
ttggtttagc attttgtcag ttttatcttc agaaattctc tgcgattaag aagataattt
                                                                        1.80
attaaaggtg gtccttccta cctctgtggt gtgtgtcgcg cacacagctt agaagtgcta
                                                                        240
taaaaaagga aagageteea aattgaatea.eetttataat ttacecattt etatacaaca
                                                                       300
ggcagtggaa gcagtttcag agaacttttt gcatgcttat ggttgatcag ttaaaaaaga
                                                                       360
atgttacagt aacaaataaa gtgcagttt
                                                                       399
      <210> 232
      <211> 397
      <212> DNA
      <213> Homo sapien
      <400> 232
ccaggataat atacacaggt ttgcagctaa aactgtgcac agtgggtcat tgatgctagt
                                                                        60
cacagtggaa ctgaaggaag gctctacagc ccagcttatc ataaacactg agaaaactgt
                                                                       120
gattggctct gttctgctgc gggaactgaa gcctgtcctg tctcaggggt aacctgctta
                                                                       180
catctggact ttagaatctg gcacacaaca aaagtgcctg gcatccacta ctgctgcctt.
                                                                       240
tcatttataa taatagccct tccatctggc agtgggggaa gaatacactc ttgacattct
                                                                       300
tgtctcctgc tttagaatgc tagtgtgtat ctatcatgta tgcaatactt tccccctttt
                                                                       360
tgctttgcta accaaagagc atatatttta ctgtcag
                                                                       397
      <210> 233
      <211> 508
      <212> DNA
      <213> Homo sapien
      <400> 233
cgaggagtcg cttaagtgcg aggacctcaa agtgggacaa tatatttgta aagatccaaa
                                                                        60
aataaatgac gctacgcaag aaccagttaa ctgtacaaac tacacagctc atgtttcctg
                                                                       120
ttttccagca cccaacataa cttgtaagga ttccagtggc aatgaaacac attttactgg
                                                                       180
gaacgaagtt ggttttttca agcccatatc ttgccgaaat gtaaatggct attcctacaa
                                                                       240
agtggcagtc gcattgtctc tttttcttgg atggttggga gcagatcgat tttaccttgg
                                                                       300
ataccctgct ttgggtttgt taaagttttg cactgtaggg ttttgtggaa ttgggagcct
                                                                       360
aattgatttc attcttattt caatgcagat tgttggacct tcagatggaa gtagttacat
                                                                       420
```



480 tatagattac tatggaacca gacttacaag actgagtatt actaatgaaa catttagaaa 508 aacgcaatta tatccataaa tatttttt <210> 234 <211> 358 <212> DNA <213> Homo sapien <400> 234 60 aaatgttggt attcaaaacc aaagatataa ccgaaaggaa aaacagatga gacataaaat gatttgcaag atgggaaata tagtagttta tgaatgtaaa ttaaattcca gttataatag 120 tgyctacaca ctctcactac acacacagac cccacagtcc tatatgccac aaacacattt 180 240 ccataacttg aaaatgagta ttttgcatat ctcagttcag gatatgtttt ttacaagtta atcctaaagt cataaagcaa gaagctattc atagtacaag attttatttg ctaagcttta 300 caaattaaac totaaaaaat tattacaatg atactgaaag atattttatt ggootttt 358 <210> 235 <211> 482. <212> DNA <213> Homo sapien <400> 235 gaagaaagtt agatttacgc cgatgaatat gatagtgaaa tggattttgg cgtaggtttg 6.0 gtctagggtg tagcctgaga ataggggaaa tcagtgaatg aagcctccta tgatggcaaa 120 tacageteet attgatagga catagtggaa gtgagetaca aegtagtaeg tgtegtgtag 180 tacgatgtct agtgatgagt ttgctaatac.aatgccagtc aggccaccta cggtgaaaag 240 aaagatgaat cctagggctc agagcactgc agcagatcat ttcatattgc ttccgtggag 300 tgtggcgagt cagctaaata ctttgacgcc ggtggggata gcgatgatta tggtagcgga 360 qqtqaaatat gctcgtgtgt ctacgtctat tcctactgta aatatatggt gtgctcacac 420 gataaaccct aggaagccaa ttgatatcat agctcagacc atacctatgt atccaaatgg 480 482 <210> 236 <211> 149 <212> DNA <213> Homo sapien <400> 236 cctcttcatt gttcacatgt cacaggagga ggctctgagc aaaggccact ggcaagttag 60 ggcaacacca agaaggctct gcggagagac tccctgtggg ttggggcctg gcaggaacgg 120 149 tgcctgtgga ctgtttatgg tctgtccag <210> 237 <211> 391 <212> DNA <213> Homo sapien <400> 237 60 gaagctaaat ccaaagaaat atgaaggtgg ccgtgaatta agtgatttta ttagctatct acaaagagaa gctacaaacc cccctgtaat tcaagaagaa aaacccaaga agaagaagaa 120 ggcacaggag gatctctaaa gcagtagcca aacaccactt tgtaaaagga ctcttccatc 180 agagatggga aaaccattgg ggaggactag gacccatatg ggaattatta cctctcaggg 240 ccgagaggac agaatggata taatctgaat cctgttaaat tttctctaaa ctgtttctta 300 gctgcactgt ttatggaaat accaggacca gtttatgttt gtggttttgg gaaaaattat 360 ttgtgttggg ggaaatgttg tgggggtggg g 391

73



```
<210> 238
       <211> 374
      <212> DNA
      <213> Homo sapien
      <400> 238
aaaaaacaaa acaatgtaag taaaggatat ttctgaatct taaaattcat cccatgtgtg
                                                                          60
atcataaact cataaaaata attttaagat gccggaaaag gatactttga ttaaataaaa
                                                                         120
acactcatgg atatgtaaaa actgtcaaga ttaaaattta atagtttcat ttatttgtta
                                                                         180
ttttatttgt aagaaatagt gatgaacaaa gatccttttt catactgata cctggttgta
                                                                         240
tattatttga tgcaacagtt ttctgaaatg atatttcaaa ttgcatcaag aaattaaaat
                                                                         300
catctatctg agtagtcaaa atacaagtaa aggagagcaa ataaacaaca tttggaaaaa
                                                                         360
aaaaaaaaa aaaa
                                                                         374
      <210> 239
      <211> 200
      <212> DNA
      <213> Homo sapien
      <400> 239
aaagatgtct ttgaccgcat atgtactgga aatttcaaac gtggatcttc ccaggttgta
                                                                          60
gtctttgtgt tatgatcaat gaagaagggc cggccgtttg gcgctatcct catttcccag
                                                                         120
ccgggtggca agaagctctg tgtgactttg tgttgtggtt tgggggagtt gtaaggtgat
                                                                         180
ggctgtgggg actgtgggtt
                                                                         200
      <210> 240
      <211> 314
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (314)
      \langle 223 \rangle n = A,T.C or G
      <400> 240
ctggtaaact gtccaaaaca aggttccaaa taacacctct tactgattta ccctacccat
                                                                          60
acatatneca natagntttt gateaaaaac atgaaatana teeacetget tattttaage
                                                                         120
atattaaaaa ggaaactaat tggaccattt tctatttgtc tattttatac aaaaaggcta
                                                                         180
cacaattgat acactctatt cagataacaa tcaattagag tgantatgaa ttactggcga
                                                                        240
caccatcact caattcttaa aaattagaaa ttgctgtagc agtattcact ataacttaac
                                                                        300
actaccgaga gact
                                                                        314
      <210> 241
      <211> 375
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(375)
      \langle 223 \rangle n = A,T,C or G
      <400> 241
```

```
ccaagtcctt ggagttatag gatattcatt acttcctctc attgtaatag cccctgtact
                                                                        60
tttggtggtt ggatcatttg aagtggtgtc tacacttata aaactgtttg gtgtqttttq
                                                                        120
ggctgcctac agtgctgctt cattgttagt gggtgaagaa ttcaagacca aaaagcctct
                                                                        180
totgatttat coaatotttt tattatacat ttatottttg togttatata ctggtgtgtg
                                                                       240
atccaagtta tacatgaata gaaaaagatg gtgttaaatt tgtgtgtagg ctgggaattc
                                                                       300
tngctaaagg aatggnaaaa aacctgtnnt tgnaaaattn acntgtccca aagnnaagga
                                                                       360
anctaaacgc ttttt
                                                                       375
      <210> 242
      <211> 387
      <212> DNA
      <213> Homo sapien
      <400> 242
aaaggcattc tctgatttac atgagaattg agaaactgag atgtatgatt tgtctgttag
                                                                        60
teaattteae accetteeat teteataage eccaaatttt geteagttaa ggagettget
                                                                       120
ttaggcccac ctatgtaagt ctgttatact agctaatgtg cccatttgaa tagttcaagg
                                                                       180
gtcagctaat gctctgagct tcatggctcc agtataaaga acaaatttaa caaaattaag
                                                                       240
ctgttactgt agccgagtta cccttctgct ccacacatat gtagtgggat cttgcaggat
                                                                       300
ttccatagtg ccaattatca aaggeettga ctaettagea ttgetgtatt acagatgtge
                                                                       360
aaactgaggc actgaaaagt caaattt
                                                                       387
      <210> 243
      <211> 536
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(536)
      <223> n = A, T, C or G
      <400> 243
aaaccaaaag gacgaagaaa aaacactttn aaaaaaaaaa aaaaaaaaga aaaaccaaac
                                                                        60
catattttgc cacatgtgag agtacggtca agcagtattt acaaaaaggt taacggaaca
                                                                       120
acactetgae acatgetetg agaatactgg gaetgetgtt teaaaaaaaa aggtteaaae
                                                                       180
ttattgtcac agcatcatca caaaatagag gatcaccatt ggtttgcttg gcttttcttt
                                                                       240
tttttttcc cccaagtgag gacctaactc caaataatac aatagaatat gcaaattatc
                                                                       300
ttcacatcaa gagtacccca agaaaaacga aatccatggc acanacactg tacaagggtg
                                                                       360
cagggcaggg ctctgagggg cccaaacccc attttgccaa ctcgattttc tagcattgaa
                                                                       420
gggagcaagg ggtcaggcat atgatggaga tgatactgaa atgatttatc caaaatccat
                                                                       480
gcaaatcaag ttctttggat agaggtgaan aacttggaca tggctgtttc aggcag
                                                                       536
      <210> 244
      <211> 397
      <212> DNA
      <213> Homo sapien
      <400> 244
ccaggataat atacacaggt ttgcagctaa aactgtgcac agtgggtcat tgatgctagt
                                                                        60
cacagtggaa ctgaaggaag gctctacagc ccagcttatc ataaacactg agaaaactgt
                                                                       120
gattggctct gttctgctgc gggaactgaa gcctgtcctg tctcaggggt aacctqctta
                                                                       180
catctggact tragaatctg gcacacaaca aaagtgcctg gcatccacta ctgctgcctt
                                                                       240
tcatttataa taatagccct tccatctggc agtgggggaa gaatacactc ttgacattct
                                                                       300
tgtctcctgc tttagaatgc tagtgtgtat ctatcatgta tgcaatactt tccccctttt
                                                                       360
```

```
tgctttgcta accaaagagc atatatttta ctgtcag
                                                                         397
        <210> 245
        <211> 508
        <212> DNA
       <213> Homo sapien
       <400> 245
 cgaggagtcg cttaagtgcg aggacctcaa agtgggacaa tatatttgta aagatccaaa
                                                                         60
 aataaatgac gctacgcaag aaccagttaa ctgtacaaac tacacagctc atgtttcctg
                                                                        120
 ttttccagca cccaacataa cttgtaagga ttccagtggc aatgaaacac attttactgg
                                                                        180
 gaacgaagtt ggttttttca agcccatatc ttgccgaaat gtaaatggct attcctacaa
 agtggcagtc gcattgtctc tttttcttgg atggttggga gcagatcgat tttaccttgg
                                                                        240
                                                                        300
 ataccctgct ttgggtttgt taaagttttg cactgtaggg ttttgtggaa ttgggagcct
                                                                        360
 aattgatttc attcttattt caatgcagat tgttggacct tcagatggaa gtagttacat
                                                                        420
 tatagattac tatggaacca gacttacaag actgagtatt actaatgaaa catttagaaa
                                                                        480
 aacgcaatta tatccataaa tattttt
                                                                        508
       <210> 246
       <211> 358
       <212> DNA
       <213> Homo sapien
       <400> 246
aaatgttggt attcaaaacc aaagatataa ccgaaaggaa aaacagatga gacataaaat
                                                                         60
gatttgcaag atgggaaata tagtagttta tgaatgtaaa ttaaattcca gttataatag
                                                                        120
tggctacaca ctctcactac acacacagac cccacagtcc tatatgccac aaacacattt
                                                                        180
ccataacttg aaaatgagta ttttgcatat ctcagttcag gatatgtttt ttacaagtta
                                                                        240
atcctaaagt cataaagcaa gaagctattc atagtacaag attttatttg ctaagcttta
                                                                        300
caaattaaac tctaaaaaat tattacaatg atactgaaag atattttatt ggcctttt
                                                                       358
       <210> 247
       <211> 673
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(673)
      <223> n = A, T, C or G
      <400> 247
gaagaaagtt agatttacgc cgatgaatat gatagtgaaa tggattttgg cgtaggtttg
                                                                        60
gtctagggtg tagcctgaga ataggggaaa tcagtgaatg aagcctccta tgatggcaaa
tacageteet attgatagga catagtggaa gtgagetaca aegtagtaeg tgtegtgtag
                                                                       120
                                                                       180
tacgatgtct agtgatgagt ttgctaatac aatgccagtc aggccaccta cggtgaaaag
                                                                       240
aaagatgaat cctagggctc agagcactgc agcagatcat ttcatattgc ttccgtggag
                                                                       300
tgtggcgagt cagctaaata ctttgacgcc ggtggggata gcgatgatta tggtagcgga
ggtgaaatat gctcgtgtgt ctacgtctat tcctactgta aatatatggt gtgctcacac
                                                                       360
gataaaccct aggaagccaa ttgatatcat agctcagacc atacctatgt atccaaatgg
                                                                       420
ttcttttttt ccggagtagt aagttacaat atgggagatt attccgaagc ctggtaggat
                                                                       480
                                                                       540
aagaatataa acttcagggt gaccgaaaaa tcagaatagg tgttggtata gaatggggtc
tectneteeg eggggtenaa gaaggtggtg ttgangttge eggnetgtta ntagtatagn
                                                                       600
                                                                       660
gatgccanca gct
                                                                       673
```

```
<210> 248
      <211> 149
      <212> DNA
      <213> Homo sapien
      <400> 248
cetetteatt gtteacatgt caeaggagga ggetetgage aaaggeeact ggeaagttag
                                                                        60
ggcaacacca agaaggctct gcggagagac tccctgtggg ttggggcctg gcaggaacgg
                                                                        120
tgcctgtgga ctgtttatgg tctgtccag
                                                                        149
      <210> 249
      <211> 458
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(458)
      <223> n = A, T, C \text{ or } G
      <400> 249
gaagctaaat ccaaagaaat atgaaggtgg ccgtgaatta agtgatttta ttagctatct .
                                                                        60
acaaagagaa gctacaaacc cccctgtaat tcaagaagaa aaacccaaga agaagaagaa
                                                                       120
ggcacaggag gatctctaaa gcagtagcca aacaccactt tgtaaaagga ctcttccatc
                                                                       180
agagatggga aaaccattgg ggaggactag gacccatatg ggaattatta cctctcaggg
                                                                       240
ccgagaggac agaatggata taatctgaat cctgttaaat tttctctaaa ctgtttctta
                                                                       300
gctgcactgt ttatggaaat accaggacca gtttatgttt gtggttttgg gaaaaattat
                                                                       360
ttgtgttggg ggaaatgttg tgggggtggg gttgagttgg gggtattttc taatttttt
                                                                       420
tgtacatttg gaacagtgac aataaatgan accccttt
                                                                       458
      <210> 250
      <211> 374
      <212> DNA
      <213> Homo sapien
      <400> 250
aaaaaacaaa acaatgtaag taaaggatat ttctgaatct taaaattcat cccatgtgtg
                                                                        60
atcataaact cataaaaata attttaagat gccggaaaag gatactttga ttaaataaaa
                                                                       120
acactcatgg atatgtaaaa actgtcaaga ttaaaattta atagtttcat ttatttgtta
                                                                       180
ttttatttgt aagaaatagt gatgaacaaa gatccttttt catactgata cctggttgta
                                                                       240
tattatttga tgcaacagtt ttctgaaatg atatttcaaa ttgcatcaag aaattaaaat
                                                                       300
catctatctg agtagtcaaa atacaagtaa aggagagcaa ataaacaaca tttggaaaaa
                                                                       360
aaaaaaaaa aaaa
                                                                       374
      <210> 251
      <211> 356
      <212> DNA
      <213> Homo sapien
      <400> 251
aaagatette tetaacaage tatgggaatt tggetteata etetteett geaacageag
                                                                        60
tgttctgggt gataattttg aattgatacc tgttcctttt tctgggtttt gttggctttt
                                                                       120
tgaaaaattg tctttcctta tcattggtgg gaggcttggt agcaaagtaa cattttttgg
                                                                       180
aaaagaggac agaaaaattg aactacagct tgagaacgta ttctttttt cctactttgt
                                                                       240
tattgcaaat tgaggaatca cttttaactg ttttaggtgt gtgtgtccag agtgagcaag
                                                                       300
```



```
gattatgttt ttggattgtc aaagaggatg cttagtctta aaataaaaat aaattt
                                                                         356
       <210> 252
       <211> 484
       <212> DNA
       <213> Homo sapien
       <400> 252
 ctggtaaact gtccaaaaca aggttccaaa taacacctct tactgattta ccctacccat
                                                                         60
 acatatecca aatagttttt garcaaaaac atgaaataga tecacetget tattttaage
                                                                        120
 atattaaaaa ggaaactaat tggaccattt tctatttgtc tattttatac aaaaaggcta
                                                                        180
 cacaattgtt acactttatt cagattacaa ttaattagag tgattatgaa ttagtgttct
                                                                        240
 acaccattac tcaattctta aaaattagaa attgctgtag cagtattcac tataacttaa
                                                                        300
 cactacgaga gacttaaaaa acagttactg caaaaaaaaa aaagagctac ttcaaagcaa
                                                                        360
 gcaaagtcag taccattaca gatattetta aaaaaaaaaa aaaatttaac aagcaagget
                                                                        420
 agggtttgat aaattccatc ttgtgatcca ttcttgtgca ttcttcactt cttgagtcac
                                                                        480
 tccc
                                                                        484
       <210> 253
       <211> 379
       <212> DNA
       <213> Homo sapien
       <400> 253
aaaaagcgct tagacttccc tttccatctg gaacatgtaa aattttgcag caacaggttt
                                                                         60
totocaatic officagoaag aattoccago ofacacacaa afficacaco afotittet
attcatgtat aacttggatc acacaccagt atataacgac aaaagataaa tgtataataa
                                                                        120
                                                                        180
aaagattgga taaatcagaa gaggettttt ggtettgaat tetteaceca etaacaatga
                                                                        240
agcagcactg taggcagccc aaaacaccc aaacagtttt ataagtgtag acaccacttc
                                                                        300
aaatgatcca accaccaaaa gtacaggggc tattacaatg agaggaagta atgaatatcc
                                                                        360
tataactcca aggacttgg
                                                                        379
      <210> 254
      <211> 387
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(387)
      <223> n = A, T, C or G
      <400> 254
aaatttgact tttcagtgcc tcagtttgca catctgtaat acagcaatgc taagtagtca
                                                                        60
aggccnttga taattggcac tatggaaatc ctgcaagatc ccactacata tgtgtggagc
                                                                       120
agaagggtaa ctcggctaca gtaacagctt aattttgtta aatttgttct ttatactgga
                                                                       180
gccatgaagc tcagagcatt agctgaccct tgaactattc aaatgggcac attagctagt
                                                                       240
ataacagact tacataggtg ggcctaaagc aagctcctta actgagcaaa atttggggct
                                                                       300
tatgagaatg aaagggtgtg aaattgacta acagacaaat catacatctc agtttctcaa
                                                                       360
ttctcatgta aatcagagaa tgccttt
                                                                       387
      <210> 255
      <211> 225
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1)...(225)
      \langle 223 \rangle n = A,T,C or G
      <400> 255
aaatgtcttg tttcccagat ttcaggaaan tttttttctt ttaagctatc cacagcttac
                                                                         60
agcacctttg ataaaatata cttttgtgaa caaaaattga gacatttaca ttttctccct
                                                                        120
atgtggtcgc tccagacttg ggaaactatt catgaatatt tatattgtat ggtaatataq
                                                                        180
ttattgcaca agttcaataa aaatctgctc tttgtatgac agaat
                                                                        225
      <210> 256
      <211> 544
      <212> DNA
     <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(544)
      <223> n = A,T,C or G
      <400> 256
ccttgcttaa agcccagaag tggtttaggc ntttggaaaa tctggttcac atcataaaga
                                                                        60
actigating adatgithing tatagasaca agigetaagi glacegiati atactigatg
                                                                        120
ttggtcattt ctcagtccta tttctcagtt ctattatttt agaacctagt cagttcttta
                                                                        180
agattataac tggtcctaca ttaaaataat gcttctcgat gtcagatttt acctgtttgc
                                                                        240
tgctgagaac atctctgcct aatttaccaa agccagacct tcagttcaac atgcttcctt
                                                                        300
agcttttcat agttgtctga catttccatg aaaacaaagg aaccaacttt gttttaacca
                                                                        360
aactttgttt ggttacagtt ttcaggggag cgtttcttcc atgacacaca gcaacatccc
                                                                       420
aaagaaataa acaagtgtga caaanaaaaa aacaaaccta aatgctactg ttccaaagag
                                                                        480
caacttgatg gttttttta atactgagtg caaaaggnca cccaaattcc tatgatgaaa
                                                                       540
tttt
                                                                       544
      <210> 257
      <211> 420
      <212> DNA
      <213> Homo sapien
      <400> 257
aaatgtettg ttteecagat tteaggaaac tttttttett ttaagetate cacagettae
                                                                        60
agcaatttga taaaatatac ttttgtgaac aaaaattgag acatttacat tttctcccta
                                                                       120
tgtggtcgct ccagacttgg gaaactattc atgaatattt atattgtatg gtaatatagt
                                                                       180
tattgcacaa gttcaataaa aatctgctct ttgtatgaca gaatacattt gaaaacattg
                                                                       240
gttatattac caagactttg actagaatgt cgtatttgag gatataaacc cataggtaat
                                                                       300
aaacccacag gtactacaaa caaagtctga agtcagcctt ggtttggctt cctagtgtca
                                                                       360
attaaacttc taaaagttta atctgagatt ccttataaaa acttccagca aagcaacttt
                                                                       420
      <210> 258
      <211> 736
      <212> DNA
      <213> Homo sapien
      <400> 258
aaacaaaatg ctaaacctaa aaacattgtt ctgtcagttc ccaaattaaa tctacttaga
                                                                        60
```



```
acaaaaacaa aaatttatag ctcggtcaca tactacttaa ataatattgt tcaggcatct
                                                                         120
 ctaaaatcct ccatgttttc aagtatggaa atagaactca aatattccac aatacagtac
                                                                         180
 taaacagatg gagtatttag gaaagacttt gttgtcatat ggcacaatat taatattttg
                                                                        240
 ttgcttcaat acgttttgaa ataaatatca gatttttgtt ttttttcct aaaagaccaa
                                                                        300
 aattataatc tacattaaga taattctgac tgtggttaag acttaagagt gtaaaataca
                                                                        360
 acatcaatat tttatcacaa aagtaaagct ggtaacaaat tataaaagga gccagtactc
                                                                        420
 tactgagaca ggctcggaga ttaaagctca tcatgataga aatagtcatc atggagctgt
                                                                        480
ctgccataat ctgtggcttc actggtgaga aacaagtccg ggttttccag aatctcttct
                                                                        540
tcagagagct ttttgtcacc attcaaatcc atttcatcaa ttagatgaag cgcctcctct
                                                                        600
tgtgcaatgc cctgattatt aggtctaccc aaggtaacag ctcttgggga tcaagcctgc
                                                                        660
catcgttatc tttgtcataa tcattcaccg aatctgtctt tctcacaagt atcccattct
                                                                        720
 ggatcttcat ttgcag
                                                                        736
       <210> 259
       <211> 437
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(437)
       <223> n = A, T, C \text{ or } G
      <400> 259
aaaaccatac tgaaatcatt taccaaataa cnaagatctt aatctaaaag atagtgaata
                                                                         60
catcatcatc atgaaatctg gttttatgtg ctctatgaag tacttggaga attgctttt
                                                                        120
tatttttctt ttgctttatt aggtcacaca aaacagaatg aattagcaga aaaatgtatg
                                                                        180
ttataaaaca gcatttacta cttcaattta attttttta ctaacaattg tggacctttt
                                                                        240
tgatgacact tatgtatgtt tttaataaat tatgtactta ttagtactta atgagccctt
                                                                        300
cctgcctcaa tataaaatta ctaaacttgg agaattacag attttattgt aggccctgat
                                                                        360
gttagtcact ttggagaagc taaaaatttg gaaatgatgt aattcccact gtaatagcat
                                                                        420
agggattttg gaagcag
                                                                       4.37
      <210> 260
      <211> 592
      <212> DNA
      <213> Homo sapien
      <400> 260
ttttttttt gaaaaatata aaattttaat aaaggctaca tctcttaatt acaataatta
                                                                        60
ttgtaccaag taattttcct taaatgaact ctttataatg cataatttac agtataagta
                                                                       120
gaacaaaatg tcatgacaaa agtcattgag tacaagactt gtaataaaaa ggcataaaat
                                                                       180
atatttatac ataaacccct ttcaaaaaac aagggaaagc ttgagccctc aatatagggc
                                                                       240
gacacacgga gcgggtgacc gtgcaggtac aggtactgta ctgatttaaa gtcaagcact
                                                                       300
agagatagtg gattaatact cttttgccgt acactatata cagatgtata gtacaagtaa
                                                                       360
caatggcaaa cagaatgtac agattaactt aacacaaaaa cccgaacatc aaaatgaagg
                                                                       420
tgtgtggagg aaaggtgctg ctgggtctcc ctacaactgt tcatttcttt gtggggcagg
                                                                       480
gggtagttcc tgaatggctg tggtccaatg actaatgtaa aacaaaaaca gaaacaaaaa
                                                                       540
aaacaaggaa ctgtcatttc cacgaaagca cagcggcagt gattctagca gg
                                                                       592
      <210> 261
      <211> 450
      <212> DNA
      <213> Homo sapien
```

WO 00/37643 PCT/US99/30909 81

<400> 261 gtggcagggc ccagccccga accagacaag ggacccctca aggagcttca ttctagcatg 60 agaaaattga gaagtaaacc agaaagttac agaatgtctg aaggggacag tgtgggagaa 120 tccgtccatg ggaaaccttc ggtggtgtac agatttttca caagacttgg acagatttat 180 cagtcctggc tagacaagtc cacaccctac acggctgtgc gatgggtcgt gacactgggc 240 ctgagctttg tctacatgat tcgagtttac ctgctgcagg gttggtacat tgtgacctat 300 gccttgggga tctaccatct aaatcttttc atagcttttc tttctcccaa agtggatcct 360 teettaatgg aagaeteaga tgaeggteet tegetaceea eeaaacagaa egaggaatte 420 cgccccttca ttcgaaggct cccagagttt 450 <210> 262 <211> 239 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(239) <223> n = A,T,C or G<400> 262 taactttgat gacaaaatct aaaattaaag anttagtctt aaaagcctat agtgacttgt 60 ttacttgcat aaataatatt ttcacttagt acaggctatt aatataagta atgagaattt 120 aagtattaac tcaaaaaaag atagaggctc caaacttttc taagaaatta atgcattttc 180 aaagtaataa tataatcaat ctgtaagtca aaagtaattt catattcatt gccaaattt 239 <210> 263 <211> 376 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(376) <223> n = A, T, C or G<400> 263 aaaaaaaaa aaaaaaaatt ccttgtngtt tnttagagga aaaaaagaaa aaccccaact 60 tttancactg atactacata ttgctctgtt aaagaatttt ctctgccaaa aaaaagaaaa 120 aacaaaaaaa cgcttaaagc tggagtttga cattctgctt tcagatgctg tctttttatt 180 agtgagtgat gatggtttgc taataatcaa taggtaataa ttttttgtaa tcccatcaag 240 tggctccata tgtttctgct ctctcgtgac tgtgttaatg tttaactgtt gtaccttaaa 300 gccgaaatca gtaactatgc atactgtaac caaggtattg ggcttacaga gttgtttgtt 360 gnataaagaa aatttt 376 <210> 264 <211> 207 <212> DNA <213> Homo sapien <400> 264 aaattagcat tccacaaata tacaggtaat ttaataatta ttgtgcatga atacatacac 60 aatgcttata tatacaaatt ccagtttgtt ttcatgtgct ggcaagggat ttgtatacaa 120 tcataagctg tgttcatatt ggtcccattg aatattcaca atacaaaagc acaaaagaac 180 cattgattta caaaaggaaa tctattt 207

```
<210> 265
       <211> 388
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(388)
       <223> n = A,T,C or G
       <400> 265
naactgcact ttatttgtta ctgtaacatt nttttttaac tgatcaacca taagcatgca
                                                                         60
aaagneenet gaaactgett ceactgeetg ttgtatagaa atgggtaaat tataaaggtg
                                                                        120
atteaatttg-gageteette etttttata gcacttctaa gctgtgtgcg cgacacacac
                                                                        180
cacagaggta ggaaggacca cctttaataa attatcttct taatcgcaga gaatttctga
                                                                        240
agataaaact gacaaaatgc taaaccaagg ctttgatgag tcccaaagga ccacagatcc
                                                                        300
atcggctcct atttgaagaa ttcatcccct gtagtgttct agcctttgta gggcactgga
                                                                        360
ttacaagatc caccagggct ctgaacaa
                                                                        388
       <210> 266
       <211> 616
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(616)
       <223> n = A,T,C or G
       <400> 266
aaatacagag tcaaaagatg atttataaaa tntaaaacat tttctgcttg gccgtatttg
                                                                        60
aagacaagct gaatacatat ctatgttctg aataagtcca ctatggatat atataggaag
                                                                       120
agatatacat atatccatcc acagatacac acacacatat atatttctgc atgtatatat
                                                                       180
acataattct ttctatagtt acaggaaata cttcttctat aattctgatt ttgactccca
                                                                       240
tcctccacca tttactcatc cactcattac ctaaatcttg gctttctttc ctatattgta
                                                                       300
aataatccat ccaaacttct agccagtact gtcaggaggg ttcttgctcg agtgagctgt
                                                                       360
taatactatt ttccactgac aacttctgca catcgaggac acagtgtatc tgaagactcc
                                                                       420
gctgtatact tccaacaacg ggggcatttt tctttcgtag tcggcatgac aattacttta
                                                                       480
taggaagact cttcacgaat atcaccacct tctaagttga tgaggaattt ccctttaagc
                                                                       540
tcgattacat ctgcagtcat ctctcgtggt tcctgaccag taaagttgac tcagaagcca
                                                                       600
tcattaattc attcaa
                                                                       616
      <210> 267
      <211> 341
      <212> DNA
      <213> Homo sapien
      <400> 267
ccattatgta tgtattttct tgaaaaatac ttatttcagc tacttatttt taatagttac
                                                                        60
ttattcttgt tgtattgtca tttgagtttt gtatatattt ttgatattaa ccccttgtca
                                                                       120
catgtataat ttgcaaatat tttctccctt tttttagttg tcacattctg ttcattgtat
                                                                       180
cagattctgt gcagcagctt tttaatttga agtgatctga ctgacttgtt cttccttttg
                                                                       240
tgtcctggga tatttaggtt aaatcaaaaa acttgctgcc cagaccaatg ttatggggct
                                                                       300
ttcactctat tttttggtag tagtagttta agagttttag g
                                                                       341
```

```
<210> 268
          <211> 367
           <212> DNA
          <213> Homo sapien
          <220>
          <221> misc_feature
          <222> (1)...(367)
          <223> n = A, T, C or G
           <400> 268
    ttgtagattg gaatagcaaa agtgaatgct ntgaccaaaa tttttgccct cctaaataaa
                                                                              60
    gacqtntcct tctagagagc aaatctatca taaaatgtca aaactagaag agaataaaat
                                                                             120
    qaaaqqaaaa aacctagaaa aatatcctaa aatatcaaat gcagtcattt ctaaatataa
                                                                             180
    gccataatta tagctttacc tattgttctt attgttccta tgctgcttct acaatgttac
                                                                             240
    atcaactata cttagcttta ctctcccaaa atcttggtga tgaagccttc tgagtgtgct
                                                                             300
    ttccaatgtg ccagaaccag aagggcattc caaggcttcc ccacatttcc tccatttacg
                                                                             360
    gagacag
                                                                             367
          <210> 269
           <211> 270
           <212> DNA
           <213> Homo sapien
           <220>
          <221> misc feature
          <222> (1)...(270)
           \langle 223 \rangle n = A,T,C or G
           <400> 269
    caaatetete ecteactaga eqtaaqeent tincteacte teteaatett atgeateata
                                                                              60
    gnaangengn tgaggtggat taaaccaaac ccagctacgc aaaatcttag catactcctc
                                                                             120
    aattacccac ataggatgaa taatagcagt tctaccgtac aaccctaaca taaccattct
                                                                             1.80
    taatttaact atttatatta teetaactae taeegeatee etaetaetea aettaaaete
                                                                             240
    cagcaccacg accctactac tatntcgcac
                                                                             270
           <210> 270
           <211> 368
           <212> DNA
           <213> Homo sapien
           <220>
           <221> misc feature
           <222> (1)...(368)
           <223> n = A, T, C or G
           <400> 270
" 'ctgaatcatg aataacacta tataatagag tntaaggaac acaagcatta gatgtgatcc
                                                                              60
    ttgccccata cccttagatt atgtcagact aaagctgaca attctgccag gctctgaacc
                                                                             120
    cctagtgccc ccaacccaaa tcttggaagc aaagaatatg ccctgtcata caactttgta
                                                                             180
    caagttgtag taaaacaaag cttaagtttt ctcatctttc tacagcaaat ggtcagttat
                                                                             240
    ttaataaaca ctaaaatgct cctaagaatc cattttgagt ttgtttacca aacacattgt
                                                                             300
    gcaagaactg actacacaaa aagttccttt gaaatttggt ccacaaattc acttaaggtt
                                                                             360
    ggaaattt
                                                                             368
```

```
<210> 271
       <211> 313
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(313)
      <223> n = A,T,C or G
      <400> 271
aaatttatat aaaactctgt acatgttcac tttattattg cataaacagc ataatcttca
                                                                        60
agacaanngt ttgcaaacac atgtccaatt caggaaaaaa aatttcacgt ttctcgtctg
                                                                       120
gcttttttct tcttttttat ttgtttggga gattcccagc tagtttcaga cttggtctgt
                                                                       180
gaaggaggca cactattttg cttggtattt gacttggatt tatctgtctc ttgtagtatt
                                                                       240
ggcggcactt gggaagagct cttgtcagaa tcactttttg ataagattac agatggctcg
                                                                       300
gtagaagtag cag
                                                                       313
      <210> 272
      <211> 462
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(462)
      <223> n = A,T,C or G
      <400> 272
aaaaaacatt tattttaata agactattgc naacacatta aaaaaactaa atagtaatat
                                                                        60
tacaaaatct atatacttgc acatttagta tttgtcaatg tgccagaggt tttcttcatg
                                                                       120
aaatttgact tctttgaagt gaaggctttt ttctatcatc tcttatagct ctgactgaat
                                                                       180
aagtettaat getttettea tgttttetat caataggggt aaateeegag geteatatgt
                                                                       240
gtacaatctg ttagagtatc ttccagctat gtcagctcta actgttaaag aagggtctac
                                                                       300
aaacatgatt ctaggcacat attgcccatc aggtgataaa ttcttatcag tggtttcatg
                                                                       360
cataaggttt agcatgatga acttattctg agccatttct tgtatttctt cattttgggc
                                                                       420
aaatactttc tttagtgctt gagagtattg acaatcctcc ag
                                                                       462
      <210> 273
      <211> 282
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(282)
      <223> n = A,T,C or G
      <400> 273
ctgatcaaag catgggatat tttaatagtn ttatacataa tatttttaca tagaaaactt
                                                                        60
tacatnncat ttcatattat ataattctgc ttattctttc aaaaatttat acatccattg
                                                                       120
ggcaaggaat ggttttcatt aaattaccaa tattaaatgc acttaatcat tgtgtatagg
                                                                       180
ttaaaccaaa gtaactatta actaactttt aggcatttta aggaggtaaa acatacattt
                                                                       240
tacacataag tatttgatgc aaatatgcag ataaaatttt tt
                                                                       282
```

```
<210> 274
      <211> 125
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(125)
      <223> n = A, T, C \text{ or } G
      <400> 274
cagecetaga ecteaactae etaaceaaen tinettaaaa taaaateeee aetatgeaca
                                                                          60
ttnaatcnct ccaacatact cggattctac cctagcatca cacaccgcac aatcccctat
                                                                         120
                                                                         125
ctagg
      <210> 275
      <211> 528
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (528)
      <223> n = A, T, C \text{ or } G
      <400> 275
aaagctgtgg aaaagcttta ttatagattt ttntacagaa ttaaaaaagt tcaaacaata
                                                                          60
ataagccngg aaccacaaat aattaaaagg aaacacagca atcccataaa caagcattct
                                                                         120
ggcatctgtt agaaattttc cctcaaatta tgaaatgtag ctctccatgc tttccaatga
                                                                         180
ttgttataat acccacaaat atctgtgatt tcagtggaat actttaacaa aagttttctt
                                                                         240
tttaaggcat gatcctgatt cattttttct tcaatatctc agtcatttca ggaactacct
                                                                         300
taaataaatc tgcaactatt ccataatctg ccacttggaa aattggagct tctgggtctt
                                                                         360
tattaattgc cacaattgtc ttgctgtctt tcatcccagc taaatgttgg atggctccag
                                                                         420
atattccaac agcaatataa agttctggtg ctactatttt tcccgtctgn ccaacttgca
                                                                         480
tgtcattggg aacaaagcca gcatcaacag cagcacggga agcaccaa
                                                                         528
      <210> 276
      <211> 420
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(420)
      <223> n = A, T, C \text{ or } G
      <400> 276
aaatgtcttg tttcccagat ttcaggaaan tttttttctt ttaagctatc cacagcttac
                                                                          60
agaaacctga taaaatatac ttttgtgaac aaaaattgag acatttacat tttctcccta
                                                                         120
tgtggtcgct ccagacttgg gaaactattc atgaatattt atattgtatg gtaatatagt
                                                                         180
tattgcacaa gttcaataaa aatctgctct ttgtatgaca gaatacattt gaaaacattg
                                                                         240
gttatattac caagactttg actagaatgt cgtatttgag gatataaacc cataggtaat
                                                                         300
aaacccacag gtactacaaa caaagtctga agtcagcctt ggtttggctt cctagtgtca
                                                                         360
attaaacttc taaaagttta atctgagatt ccttataaaa acttccagca aagcaacttt
                                                                         420
```

```
<210> 277
       <211> 668
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(668)
       <223> n = A,T,C or G
       <400> 277
 ccagggtggc tctgatatag cagccctggt ntattttcga tatttcagga agactggcag
                                                                         60
 atngcaccag accetgaatt cttctagete etccaatece attttatece atggaaccae
                                                                        120.
 taaaaacaag gtctgctctg ctcctgaagc cctatatgct ggagatggac aactcaatga
                                                                        180
 aaatttaaag ggaaaaccct caggcctgag gtgtgtgcca ctcagagact tcacctaact
                                                                        240
 agagacagge aaactgcaaa ccatggtgag aaattgacga cttcacacta tggacagett
                                                                        300
 ttcccaagat gtcaaaacaa gactcctcat catgataagg ctcttacccc cttttaattt
                                                                        360
gtccttgctt atgcctgcct ctttcgcttg gcaggatgat gctgtcatta gtatttcaca
                                                                        420
agaagtaget teagagggta acttaacaga gtateagate tatettgtea ateceaacgt
                                                                        480
tttacataaa ataagagatc ctttagtgca cccagtgact gacattagca gcatctttaa
                                                                        540
cacagoogtg tgttcaaatg tacagnggtc cttttcagag ttggacttct agactcacct
                                                                        600
gttctcactc cctgttttaa ttcaacccag ccatgcaatg ccaaataata gaaattgctc
                                                                        660
cctaccag
                                                                        668
      <210> 278
      <211> 202
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(202)
      <223> n = A,T,C or G
      <400> 278
aaattggtat cgacggcaac caggggaagn tnctaaactc ctaatctatt ctggatccaa
                                                                        60
ttngcnaagt ggggtcccat caaggttcag tggcagtgga tctgggacag atttcactct
                                                                       120
cacgatcage agtetgeaac eegaagattt tgeaacttae taetgteaac agagttaeat
                                                                       180
gtccccgtac acttttggac cc
                                                                       202
      <210> 279
      <211> 694
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(694)
      <223> n = A,T,C or G
      <400> 279
ctgtacttgg acaaaataag ttaattctat ttggttgtcc attaaagttt tatgtggcta
                                                                        60
tgnacccact ggagctaaaa attggctttt aactgtttcc aaatcagaac tagcagagga
                                                                       120
gagaagtaaa taaagccaat ggcactccct tcagaggctc aaaatggtta gattttgatg
                                                                       180
```

```
cagatttaac cttagcgagt ttcagtcagt ccatttagat gatcctgtag gttcatacaa
                                                                        240
atacactgaa ccgttggttt aacttctctt ccttcctcaa agtttatgat aaagagactc
                                                                        300
atccctgtat tgggagtgac tgacataagt tcagatctgc tcagagtggc tggtaaqqaa
                                                                        360
cacttaaggt cagtcagaaa ataatcaaac agacttctca tgtaagcacc gtgactcaca
                                                                        420
actaagacac tggctgctaa tcctggaata ccgctgtctg aattaacttt agagctgtga
                                                                        480
ttttttccta aaggaaatat ctctgccaaa gaagtttcca gacagntgct tgggagatcc
                                                                        540
ttggggaaaa ctggtctttt tgatccggtt ctttcangan taggtngaca aaagaaatnc
                                                                        600
aaaaaagnct atcccacgcn tttntcacct gggcccagcg gnnctcctcc nggggggggn
                                                                        660
aaacacangg gactcttccc ngggctngct tnng
                                                                        694
      <210> 280
      <211> 441
      <212> DNA
      <213> Homo sapier.
      <400> 280
aaaaaacttc catgcaactt ctggtttatt gtttggcaac tccacatgat aaaaaaataa
                                                                        ٤٥
aaacagccca accgagtttc ggaattaagt actcttctag taagtgattc aaacttqtaa
                                                                        120
tatttgccac aggactgact tatttattta ctagctagaa gctcttaagt tcacttgttt
                                                                        180
atcagggcat atacagaagg gtttgttaaa actcgatgtt aactttacaa ctttctqacc
                                                                       240
tggtgcatga attctcaagt actgtatttc actgtgttgg tgtgtctgat ggaaatttcg
                                                                       300 -
aygtggtccc acaaaaatat tttatgtagt gtgccttcaa agagaaccat ttatttctct
                                                                       360
tcacttatcg tcccacaaag tcacatttgg tggtgytcag ccaagtcgca tctqqtctaq
                                                                       42.0
ttttactctt gtcccaattt t
                                                                        441
      <210> 281
      <211> 398
      <212> DNA
      <213> Homo sapien
      <400> 281
aaatttgtta ggtctgaaga atctaaaact gttaatttaa cccttaactt gtgcctagaa
                                                                        60
actacagcac atataaaata tgtaaacacc agcctgttgc tgtacttttc tgcttatttt
                                                                       120
acagcetcaa atatttetca ttatettgte acttagttet teatgtttet eettetgaet
                                                                       180
tttaataatg gtaataggaa aacaaaaccc aaagcttttc agaacttcag tgtgaggttt
                                                                       240
cctattttga caagttaact tgtaaatact caggttttac gatgtataat ttacctaata
                                                                       300
gaccaaacta actcatggag atattttgaa ctattattta ggtacaaact ttataaagaa
                                                                       360
tgttagtatg tcataaaata taacattaca gcttattt
                                                                       398
      <210> 282
      <211> 226
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(226)
      \langle 223 \rangle n = A,T,C or G
      <400> 282
aaaacaatat tototttttg aaaatagtat naacaggoca tgcatataat gtacagtgta
                                                                        60
ttacnccaat atgtaaagat tcttcaaggt aacaagggtt tgggttttga aataaacatc
                                                                       120
tggatcttat agaccgttca tacaatggtt ttagcaagtt catagtaaga caaacaaqtc
                                                                       180
ctatctttt ttttggctgg ggtgggggcg cccaggccga ggctgg
                                                                       226
```

```
<210> 283
      <211> 358
      <212> DNA
      <213> Homo sapien
      <400> 283
aaacaaaaat actcaagatc atttatattt ttttggagag aaaactgtcc taatttagaa
                                                                        60
tttccctcaa atctgaggga cttttaagaa atgctaacag atttttctgg aggaaattta
                                                                        120
gacaaaacaa tgtcatttag tagaatattt cagtatttaa gtggaatttc agtatactgt
                                                                       180
actatecttt ataagteatt aaaataatgt tteateaaat ggttaaatgg accaetggtt
                                                                       240
tottagagaa atgittitag gottaattoa ticaattgio aagtacacti agiottaata
                                                                       300
cactcaggtt tgaacagatt attctgaata ttaaaattta atccattctt aatatttt
                                                                       358
      <210> 284
      <211> 288
      <212> DNA
      <213> Homo sapien
     <400> 284
aaaacttttg ttaagaaaaa ctgccagttt gtgcttttga aatgtctgtt ttgacatcat
                                                                        60
agtotagtaa aattitgaca gigcataigi acigitacta aaagotitai aigaaattai
                                                                       120
taatgtgaag tttttcattt ataattcaag gaaggatttc ctgaaaacat ttcaagggat
                                                                       180
ttatgtctac atatttgtgt gtgtgtgtgt gtatatatat gtaatatgca tacacagatg
                                                                       240
catatgtgta tatataatga aatttatgtt gctggtattt tgcatttt
                                                                       288
      <210> 285
      <211> 629
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(629)
      <223> n = A, T, C or G
      <400> 285
cctaaaagca gccaccaatt aacaaagcgt ncannctcaa cacccactac ctaaaaaatc
                                                                       60
ccaaacatat aactgaactc ctcacaccca attggaccaa tctatcaccc tatanaagaa
                                                                       120
ctaatgttag tataagtaac atgaaaacat tctcctctgc ataagcctgc gtcagattaa
                                                                       180
aacactgaac tgacaattaa cagcccaata tctacaatca accaacaagt cattattacc
                                                                       240
ctcactgtca acccaacaca ggcatgctca taaggaaagg ttaaaaaaaag taaaaggaac
                                                                       300
teggeaaate traceeegee tgtttaceaa aaacateace tetageatea ceagtattag
                                                                       360
aggcaccgcc tgcccagtga cacatgttta acggccgcgg taccctaacc gtgcaaaggt
                                                                       420
agcataatca cttgntcctt aattagggac ctgtatgaat ggcttcacga gggttcagct
                                                                       480
gtctcttact tttaaccagt gaaattgacc tgcccgtgaa gaggcnggca tgacacagca
                                                                       540
agacgagaag accctatgga gctttaattt attaatgcaa acagnaccta acaaacccca
                                                                       600
caggicctaa actiacccaa accciggca
                                                                       629
      <210> 286
      <211> 485
      <212> DNA
      <213> Homo sapien
      <400> 286
aaatgtactt gctcagctca actgcatttc agttgtatta tagtccagtt cttatcaaca
                                                                        60
```

```
ttaaaaccta taqcaatcat ttcaaatcta ttctgcaaat tgtataagaa taaagttaga
                                                                       120
attaacaatt ttattttgta caacagtgga attttctgtc atggataatg tgcttgagtc
                                                                       180
cctataatct atagacatgt gatagcaaaa gaaacaaaca aaagccagga aaacactcat
                                                                       240
tttcgccttg aatatgtaaa tgggattaat tttgtcctgt gccttatgtg gaaaggaact
                                                                       300
tctttggttt tccttttttg ttctggtgga agcatgtgca ggagacatat catccaaaca
                                                                       360
taaaccatta aaatgtttgt ggtttgcttg gctgtaattt tcaaagtagt taattgagga
                                                                       420
                                                                       480
caaagggtaa tgcagaagtg atagctttgg tttgctgagt cttgttttaa gtggccttga
                                                                       485
tattt
      <210> 287
      <211> 340
      <212> DNA
      <213> Homo sapien
      <400> 287
cctggagtcc aataaccacc ccctcatacc acaccctgtg catacaccag ccaagccttt
                                                                        60
cctggtctgg gaagggaaga gaaaaaagac gcaggccacc tgggggttct gcagtctttg
                                                                       120
gtcagtccag cottotatot tagotgcott tggottccgc agtgtaaacc ttgcctgccc
                                                                       180
ggaggcagga ggcccagctg gacctccgag ggccatgagc aggcagcagc catcttggcc
                                                                       240
tcaagcttgc ctttcccttg agtccctctc tcccctcggc tctagccaga ggtgtagcct
                                                                       300
                                                                       340
gcagatctag gaagagaaga gctggggagg aggatgaagg
      <210> 288
      <211> 290
      <212> DNA
      <213> Homo sapien
      <400> 288
                                                                       .60
aaacagtete teeteggtgt teteettgte aaactgttea teecagttte etetgaaata
gacagcattc accagaacca gccttgtcaa tggatccact gagcccggag agagcaactc
                                                                       120
                                                                       180
cqcaatttta cettetgtet tttcagetac ccaggtgttt atgtgtttte tggaettete
tacggcgctg ataaagtcaa gctcctccat ctctgcttgg tagaattttt ggcaggaatc
                                                                       240
tctaaaagat gagaggaaat cacaagactt ttccccaaag agcctgttgg
                                                                       290
      <210> 289
      <211> 404
      <212> DNA
      <213> Homo sapien
      <400> 289
ccacccacge traggreece atcacactga tgactccggg trttggcgage acaggagege
                                                                        60
aaaccttttc acattctttc tgtgatccaa atttgttttc gtttccacca caacctccat
                                                                       120
accagaatct tgcacagctt ttggtgtttg gatcatagta ccattttaat atgaaatccc
                                                                       180
tgcaagttcc ttcgtctttc ggcaacttgc atatatctgt ttcagtgaga gccaatggtt
                                                                       240
ctgtgctcac cattagattg atggttgaac tagaagctga ccttgctggc tgtggaggtg
                                                                       300
ggggctgaga tttctttgta ctgaaacttc cgtggtaggt ggctctgacc tgagacctca
                                                                       360
                                                                       404
ggtagcagac cacagccaca tggtatgtct gcccagcgag cagg
      <210> 290
      <211> 384
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
```

```
<222> (1)...(384)
      <223> n = A,T,C or G
      <400> 290
ccaggcgctc cttgtcggca tcagggaggg tggccttgaa ctgctcatgg gctgtggtca
                                                                        60
gtccctggat ctcctcaatg gtgtgcacaa tgaaggtgtc ctgcaggtcc tccatggccc
                                                                       120
cctccatcca gttgttgaag ggtgcagccc gcttggcata ctccaagtac agctggtcaa
                                                                       180
tggtctccag cagtttctcg gtccgctcca gagcttccct tcgcttctga gttagggccc
                                                                       240
ccagattgtc ccactggtca cagatctttt ggcaacgggc gttgacactg ggtgagtcat
                                                                       300
aatantccag ctcattgagc tcctgtgcga tggcggcaat ctgctccaca cggtcctggt
                                                                       360
gggcagccag gccactctcg aagg
                                                                       384
      <210> 291
      <211> 278
      <212> DNA
      <213> Homo sapien
      <400> 291
aaagtttatt titactatti cittatcact tiatigtatc atcaccatig gittcataat
                                                                        60
gtaaatacta tatgttgaac aaattaaatg tcaaaatttt.ttattaccat agtccatgtt
                                                                     . 120
aatagtgggg ctttcaggtg tttagagatt ttttttgttg ttgttaacat tcattgcaaa
                                                                       180
agtactagat ggtgtataac tctagagttg aattttaagg gattccctaa tatgtatact
                                                                       240
atctttttat ctgaagtaat aaataaacaa tgatcttg
                                                                       278
      <210> 292
      <211> 177
      <212> DNA
      <213> Homo sapien
      <400> 292
cettggeeeg gteattettg teeagtttga taggtteagg aaattegttg tacageteea
                                                                        60
cotcogttte digettaagt geatteegtg caategtetg.gaacgeetge tecaegttga
                                                                       120
tggcctcctt ggcactggtc tcaaagtagg gaatgttgtt tttgctgtag caccagg
                                                                       177
      <210> 293
      <211> 403
      <212> DNA
      <213> Homo sapien
      <400> 293
aaaaagaagg acttagggtg tcgttttcac atatgacaat gttgcattta tgatgcagtt
                                                                        60
tcaagtacca aaacgttgaa ttgatgatgc agttttcata tatcgagatg ttcgctcgtg
                                                                       120
cagtactgtt ggttaaatga caatttatgt ggattttgca tgtaatacac agtgagacac
                                                                       180
agtaatttta totaaattac agtgoagttt agttaatota ttaatactga otcagtgtot
                                                                       240
gcctttaaat ataaatgata tgttgaaaac ttaaggaagc aaatgctaca tatatgcaat
                                                                       300
ataaaatagt aatgtgatgc tgatgctgtt aaccaaaggg cagaataaat aagcaaaatg
                                                                       360
ccaaaagggg tcttaattga aatgaaaatt taattttgtt ttt
                                                                       403
      <210> 294
      <211> 305
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
```

```
<222> (1)...(305)
      <223> n = A, T, C \text{ or } G
      <400> 294
60
tatgggtgga agttggagag aaggacattt tggctttgta catgaaaaga ctctccagat
                                                                   120
agaaacagat tctgcccata agtgaaataa aatgctttgt gggggtaatg agtgacttat
                                                                   180
agtattcagg cagatgttac ataactgcta attaagtttc cctggattga ntttanncaa
                                                                   240
anaattgaaa gtngattttg gtcangtgtc agnaaactac tgcctataaa cccatatcnt
                                                                   300
                                                                   305
      <210> 295
      <211> 397
      <212> DNA
      <213> Homo sapien
     <220>
      <221> misc_feature
      <222> (1)...(397)
     <223> n = A, T, C \text{ or } G
     <400> 295
cctatctggt tggccttttt gaagacacca acctgtgtgc tatccatgcc aaacgtgtaa . . . 60
caattatgcc aaaagacatc cagctagcac gccgcatacg tggagaacgt gcttaagaat
                                                                   120
180
cotgitating granticing acquiragata tittititico arggineca aangitacota
                                                                  240
agtatatgat tgccgagtgg aaaaataggg gacagaaatc aggtattggc agtttttcca
                                                                  300
tttncatttg tgggngaatt tttaatataa atgcggagac gtaaagcatt aatgcnagtt
                                                                  360
aaaatgtttc agtgaacaag tttcagcggt tcaactt
                                                                  397
     <210> 296
     <211> 447
     <212> DNA
     <213> Homo sapien
     <400> 296
ccatcctcga tgttgaagtt gtcgtggggc ccgaagacgt tggtggggat gacagcggtg
                                                                   60
aaggtgcagc cgtactgctg gaagtaggcc ctgttctgca cgtcgatcat cctcttggca
                                                                  120
tacgagtacc caaaattgct gttgtgggga ggcccattgt ggatcatggt ctcatctatc
                                                                  180
gggtaggtcg tcttgtcagg gaagatacag gtggacaggc aggacaccac cttgcgggcg
                                                                  240
cccacctcga aggccgagtg caggacgttg tcgttcatgt gcacgttttt cctccagaag
                                                                  300
tccaaattgt atttgatatt ccggaacagg ccccccacca ttgcagcaag atggatgacg
                                                                  360
tgtgtgagtt ggaccttctc aaacagggcg cgggtctgtg ctgtatccgt gagatcggcg
                                                                  420
tctttagagg agacaaacac ccagtcc
                                                                  447
     <210> 297
     <211> 681
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(681)
     <223> n = A, T, C \text{ or } G
```

```
<400> 297
aaataacagc atgtaaaata ttaaaataca agctttcaaa aataaataca taaataagta
                                                                      60
gaaccetegt aagaaatagt caaacacatt aagteettte cagetgteee tagaaagetg
                                                                     120
ctgttctctt tttcattttc agctctggta agggcaggga ccaccctgca ggaagtgtca
                                                                     180
atgatacget gataagette ttaettetet eetgteagtt ggtgeteece etgtgatgag
                                                                     240
aaaagggtta ctgttgcagg tgctaaggaa ggctgctctt ctgtcactct gaagttgctt
                                                                     300
ggagggatgt ccccatgcag actctctccc agccctccac tcagggaagg tctgtctgta
                                                                     360
cccactgcct tctatagcag aaaacttgca ctcctgaatg ctttttttt ttttcaagaa
                                                                     420
agaagnggct gnggactcaa ctagattctt ggtttgaaaa agccaaaaca tattggtcac
                                                                     480
tgattgtcac attgggttag aaatgtccat tcatgatctc ccttaagctg cacacaaccc
                                                                     540
tatgaaataa ctaccattat ctaccctatt ttgctaaagc tcaaagagat taaataatgt
                                                                     600
tgacagggat cttagccttg aactcactga aggngttact gcaaagttct gctcttcacc
                                                                     660
                                                                     681
aagaaggntt acaggccaaa g
      <210> 298
      <211> 353
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
       <222> (1)...(353)
       <223> n = A,T,C or G
       <400> 298
 60
 geoceaenet gnecectede tgeocecaeg tetecageaa cacaaggegg ceagtggace
                                                                      120
 gtgaaccatt tatttccaaa ctataaagaa acctgctctc tgagaaaana cactgcccag
                                                                      180
 gngatgaagc tccagcccct ggaggtccaa aacccagtcc aaactcagtc cctttagaaa
                                                                    240
 gctgctgtgc cttggaaatg annntcggnt gtcanagcct gggaagtggt gggaagaacc
                                                                      300
 agcccactcc cctctcctgc tgcgattcca gcgcncgttg ggnccagatc tgg
                                                                      353
       <210> 299
       <211> 560
       <212> DNA
       <213> Homo sapien
       <400> 299
 aaagttcaag gactaacctt atttatttgg gaaaggggag gaggaaggaa atgatatggt
                                                                       60
 acccagacac tgggctaggc tgcaacttta tctcatttaa tactcccagc tgtcatgtga
                                                                      120
 gaaagaaagc aggctaggca tgtgaaatca ctttcatgga ttattaatgg atttaagagg
                                                                      180
 gcatcaatca gctcaactca agatttcata atcattttta gtatttagat tgtgcctcaa
                                                                      240
 agttgtagta cctcacaata cctccactgg tttcctgttg taaaaacctt cagtgagttt
                                                                      300
 gaccattgtg ctcttggctc ttgggctgga gtaccgtggt gagggagtaa acactagaag
                                                                      360
 tetttagtac aaaactgete tagggacace tggtgattee tacacaagtg atgtttatat
                                                                      420
 ttctcataaa gagtcttccc tatcccaagg tcttcatgat gccagtagcc atatatgata
                                                                      480
 aattatgttc agtgataact tagttatcag aaatcagctc agtggtcttc cccgccatga
                                                                      540
                                                                      560
  ttcacatttg atgagttttt
        <210> 300
        <211> 165
        <212> DNA
        <213> Homo sapien
        <220>
```

```
<221> misc feature
      <222> (1)...(165)
      <223> n = A, T, C \text{ or } G
      <400> 300
aaaaactaca taggggtgtg tgtgtgtgtg tatgtttatt ttatacacac atatttgtat
                                                                        60
attctaatat attactaagg caattttaat gaattaccat gtatataaaa aaatatctgn
                                                                       120
cacttggcac acaggtttgt atgtatgtgt atatatat gtatg
                                                                        165
      <210> 301
      <211> 438
      <212> DNA
      <213> Homo sapien
      <400> 301
aaaatatatg tatttaaaaa caaaaagcaa cagtaatcta tgtgtttctg taacaaattg
                                                                        60
ggatctgtct tggcattaaa ccacatcatg gaccaaatgt gccatactaa tgatgagcat
                                                                       120
ttagcacaat ttgagactga aatttagtac actatgttct aggtcagtct aacagtttgc
                                                                       180
ctgctgtatt tatagtaacc attttccttt ggactgttca agcaaaaaag gtaactaact
                                                                       24C
gcttcatctc cttttgcgct tatttggaaa ttttagttat agtgtttaac tggcatggat
                                                                       300
taatagagtt ggagttttat ttttaagaaa aattcacaag ctaacttcca ctaatccatt
                                                                       360
atcetttatt ttattgaaat gtataattaa ettaaetgaa gaaaaggtte ttettgggag
                                                                       420
tatgttgtca taacattt
                                                                       438
      <210> 302
      <211> 172
      <212> DNA
      <213> Homo sapien
      <400> 302
ccaaaacagg agtcctgggt gatatcatca tgagacccag etgtgctcct ggatggtttt
                                                                        60
accacaagte caattgetat ggttaettea ggaagetgag gaactggtet gatgeegage
                                                                        120
tegagtetea gtettaegga aaeggageee acetggeate tateetgagt tt
                                                                       172
      <210> 303
      <211> 552
      <212> DNA
      <213> Homo sapien
      <400> 303
ccagcetgtt gcaggetget tegtageggg egteggetge ggaetteeet teeegggtet
                                                                        60
ggatcttttc atcctaccag atgagaaagg gaatgagtga atggagtgac cccgcaccct
                                                                       120
gtcactttcc tgagacatga ctgccaggaa gaagagctgc tctggtctcc atcagggctg
                                                                       180
gcaggacaaa ctgaccagtg agtcagtagg cagagttcac actgaaaaaag ggcacaaggg
                                                                       240
ctgtcccaca atgggaggaa atggggtctc agaacttcta cttctctgaa aactaagaca
                                                                       300
caattqqqac aaccaccacc cccgtgtgag atttctcacc tcgagacagg acaagatgaa
                                                                        360
gttcacggct tcttctgggg taaagacctt gaagagccca tcacaggcca acaaaatgaa
                                                                       420
cctacaacac cagggagaaa tataaacggg ttttaggccc aaccaaaaaa taaaaaataa
                                                                       480
aaaaagggcc tggagatgga gataaaataa atatttgtcc aactattcaa aggctaaggt
                                                                       540
ttttttttt tt
                                                                        552
```

```
<211> 601
```

<210> 304

<212> DNA

<213> Homo sapien

<pre><400> 304 cctttgattc ttggtagtac attgcatgta aaatgtttat aagaagctac ttttccttc tgggaagaaa ttcccacatg agattcataa attcttagac tccgtggctt ctttggtcg gaatgcttaa actcatatga gtgttctgga tcccagtgta tccaatcata attcacatt tcaccttcac gaaccacata ctttgcccac ggtgaaatac gatacaagat ctctccgct ttactagtaa taactacctt taatttggat ccatgaggca cgagtacaga tttattctg tttggtggga tatacagctc ccatttcca taatccagtt ttttgtatgg gtacgaaaa ggattccaac cattaaaatc tccagtaaga aaaactcctt ctgctcccgg ggcccattoga </pre>	120 130 140 150 160 170 180 180 180 180 180 180 180 18
ttgcagtata aaccaccatc agcacatctg tggacgccaa atgattcata gcctctgga aacttatcaa taccaccttc attttctcca atgttcttca aaatttggct aaactgctt tacctgcgct ggaagtccac ggcgtagggc ttcaagtacc ggtcgatctc caggagtct g	a 540
<211> 401 <212> DNA <213> Homo sapien	
<400> 305 aaataacagc atgtaaaata ttaaaataca agctttcaaa aataaataca taaataaggaaccctcgt aagaaatagt caaacacatt aagtcctttc cagctgtccc tagaaagccctgttctctt tttcattttc agctctggta agggcaggga ccaccctgca ggaagtgtcaaaaagggtta ctgttgcagg tgctaaggaa ggctgctctt ctgtcactct gaagttgccgagggatgt ccccatgcag actctctccc agccctccac tcagggaagg tctgtctgcccccccccc	120 ca 180 ag 240 ct 300
<210> 306 <211> 313 <212> DNA <213> Homo sapien	
<400> 306 aaactgacta tggattcctt gaaggtctgg cagttgttga tgatggcgat catgtact acgtagcagt gagggtgctg ccgattcctc aggtgctctt ctttatacag ctgcgctt tctttatatc tgaggacaga caggcttcgg tcagacagca ctaagggcaa catggagctttcaaatgc cacgctgacg tcacgcctgg cctgaaattt cacatcacta acatctga ggatgagcct ctaaaaaataa aacaatcttt agacgatcca gactaatgga aggacaga ggttgattac ttt	ca 120 tg 180 cc 240
<210> 307 <211> 366 <212> DNA <213> Homo sapien	
<pre><220> <221> misc_feature <222> (1)(366) <223> n = A,T,C or G</pre>	
<400> 307 aaagatgctg ntaatgaaca ttacggacaa ttcatggtgt ggctagttgg taacactt gctgattttt cttatgagat ggaaaaaaaa aatcagccaa gtaagggcac atcttcac catttataag tcagcatcca aggtaaaaga attctctgtt ggacttgaca tcactccc	tt 120

```
cctctgatac tcgcctactc tcttctcaaa gaagttagnt ctttccttcc antqaaatat
                                                                        240
tctcataaaa gtcaaatggg ttctctactc tgaaaacctt gctaaaaccc aattccagca
                                                                        300
taagtttgtc tgncacaaac ncaatgnatt gcttcattaa antqcaattc atcccaatga
                                                                        360
acttcc
                                                                        366
      <210> 308
      <211> 534
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(534)
      <223> n = A, T, C \text{ or } G
      <400> 308
ccagctatca getgategte ttetgtetgg acgetegtee tgettetgae atcaaaatet
                                                                         60
totgtotcaa agtoagagto atocaactoo toaggggtoo ttatoatoag cactgottto
                                                                        120
ctgatgtccc ggatgccatc atataccagg cgggaagcat cgataaactc attctcatcc
                                                                        180
atgggctggg cagggtccga gctgagggct tccacggctg cttctacttg ctcagtaaaa
                                                                        240
cgtggcatga ctgtgttgga gagcagctta gtggcttcca gaaccttctc tgtgtagact
                                                                        300
cotggeteat agtogtocat ctotgaggtg actacgtgaa tgacceggge tgeceggect.
                                                                        360
cgaattgcac cagctgtgcg gccaggccat ccacatcctt ctcttggaga gcaatgacac
                                                                        420
atttggtcac atcttccaaa atgtgattct ctgagacagc caagaagtca tcaatggaag
                                                                        480
taatgncatc gacagcatct gtgagaacac cgacttgttt ttccattgnt cttt
                                                                        534
      <210> 309
      <211> 164
      <212> DNA
      <213> Homo sapien
      <400> 309
catacteett acactattee teateaceea actaaaaata ttaaacacaa actaceacet
                                                                        60
acctccctca ccaaagccca taaaaataaa aaattataac aaaccctgag aaccaaaatg
                                                                        120
aacgaaaatc tgttcgcttc attcattgcc cccacaatcc tagg
                                                                        164
      <210> 310
      <211> 131
      <212> DNA
      <213> Homo sapien
      <400> 310
aaaaatcatt tatctttcgg tgcttcaaca tgatgccaaa caaaaatcta ctgaataaaa
                                                                        60
atagcaagga agggaatcaa acatttataa gatatattta ttatttttct gaccaaagtq
                                                                       120
caatgatttt t
                                                                       131
      <210> 311
      <211> 626
      <212> DNA
      <213> Homo sapien
      <400> 311
cctatgtgcg ccagtttcag gtcatcgaca accagaacct cctcttcgag ctctcctaca
                                                                        60
agctggaggc aaacagtcag tgagagtgga ggctccagtc agacccgcca gatccttggg
                                                                       120
cacctggcac tcaagcactt tgcacgatgt ctcaaccaac atctgacatc tttcccgtgg
                                                                       180
```

```
agcaacttcc tgctccacgg gaaagaggtc gatggattta cccctggacc cataagtctg
                                                                       240
ttcatcctgc tgaagtcccc tccccattgc tccttcaagc caaaactaca ctttgctqqt
                                                                       300
tcctgtcccc tctgagaaag gggatagaaa gctccttcct ctatgtcctc ccatcgagat
                                                                       360
ctgttctggg gatggagctt ccaacttcct cttgcagcag gaaagaatgc tgctcaccct
                                                                       420
tetgtettge agagtgggat tgtgggaggg attggcagee ttetteteea ceacetgtee
                                                                       480
agetteetee tggteaggge tgggaeceee aggaatatta tgttgeegtg tgtgtgtg
                                                                       540
tgtgtgtgtg tcttctttta gggagcagga gtgcatctgg taattgaggg tagatgttgt
                                                                       500
gtgtgctggg gaggggtcct tctgtt
                                                                       626
      <210> 312
      <211> 616
      <212> DNA
      <213> Homo sapien
      <400> 312
aaaccaaaga aattaagaaa aaagacttca ttgcttgaat gacgcgaaca gctgtctgag
                                                                        60
tcacctagac tttaacacca cctggggccc tgggaatgac gctgacgaga gatctgcaca
                                                                       120
tagtaggcgt gggctccaaa tgtgctcatc agctgacttc acatcctcac aagtcagcct
                                                                       180
cagatatgac ccaagggata cgtaccatct cttcttgaaa cagcgtgtca aattatatat
                                                                       240
atgtatgcaa aaaagagtaa tgtactaagc aaaccaagtt tcgtcttttt cttctgaatc
                                                                       300
tggttttaat gtgacetgte atececatet ttegaattta tgageteeat ettetetaga
                                                                       360
ctgttaactt cttgaggaaa acatgctatt ttaccacctt tcactgctga atccctagcc
                                                                       420
cttaagcaca gtctctggca cagaataaat acgaaatgaa tgagtgaatg aatggatgga
                                                                       480
tgggtgaaga gaaaaggcaa tgcacaagat ttacctatca aaatccacca atggtcctta
                                                                       540
asaatggttt tgtcagtaga gatgctgaat stattcatat aatacattta tttcsatact
                                                                       600
attaagaatt ctagtg
                                                                       616
      <210> 313
      <211> 553
      <212> DNA
      <213> Homo sapien
      <400> 313
aaaaaatggc agcattgtac ttgaatcaga aagcttactg ggatttcctc atcgaaagta
                                                                        60
gagattgcag ctaatcctag taccttttgt tagtaattac ttaaggcaca gtgcaaagtt
                                                                       120
gaaggactgt tttggtacaa actcaagcca gctacatgta tgcttgcctt ggtatccttq
                                                                       180
ctagagcaca tgcgggtata ataccgtatt atacacaaca aggccaccct gttgtatctg
                                                                       240
tgttacaatt aaacatcagt cccagaaagt gaaccctagt catttattat aggtgcccac
                                                                       300
ctctgacttg gaacaaaatg ccactccatt catgttcatt tttgtcctgg agaggattta
                                                                       360
tttcctaaaa gattctgaaa gccaacaaat caatgtagtt cttcatagag aacttaagag
                                                                       420
taaggctcaa aatggcctca aaatgggctt cttggatgac ttccaacagt gactggcctt
                                                                       480
ctcaacactg cagatgtctg agcactacca taacctaacg aagtgaggaa ggaggaggca
                                                                       540
aattggtatt ttt
                                                                       553
      <210> 314
      <211> 330
      <212> DNA
      <213> Homo sapien
      <400> 314
ccagegacte cageggtgge ageaggeagt geacgtacte tgggcetece accagggtag
                                                                       60
tgaaggttcc cagctgttct gccagggcca ggaggacctc atcttcatca tagatggtat
                                                                       120
ctgtaaggaa aggcagaagc tcacttcggg tcctttcaac cccaagggcc aaggcgatgg
                                                                      180
tggacagett ettgatgetg ttgaggegaa getgaaegte eteattgegg agttegteta
                                                                      240
tgagcaccgc gatggggtac agcgagtcgt cgccgtcggc cgccgccatc ttggctccgt
                                                                      300
```

ccetttectg teagactgeg gecagegetg		330
<210> 315 <211> 380 · <212> DNA <213> Homo sapien		
<400> 315 aaaaatgaca ttgcgtttag cttattgtaa gaggttgaac tttaagccct tcagtttata attcatataa aatgcctttt ttaatcagtg catgaaattt gctttttaa agttcatttg	gtatttaaaa taatcctatt	60 120 180
aaagaaatga ttttggtaat gttgagaggt accttaccac ttcatggtta ttttcaaaag aattatgact cttccccaaa ataaacctat aaagctgatt tgcatattta caaaattttgcatatatgta tataatttt	aaatcctaac tgtaagtgta agaatcctaa aaaacttgta	240 300 360 380
<210> 316 <211> 222 <212> DNA <213> Homo sapien		
<400> 316 aaactacaga gggttttcca gctattattt cctttagttt	craaaadtaa coacttatat	6.0
taatgtttta taaaagatag tgatgaaaaa aaggtaatgc		120
aaatatttaa ggacaacata aggtattaat attggaaaaa		180 222
acaacactga aatattgcag cagtgtttaa ctgaattgtt		222
<210> 317 <211> 490 <212> DNA		
<213> Homo sapien		
<213> Homo sapien <400> 317 · ccttgaatga gcgtggagag cgattaggcc gagcagagga	gaagacagaa gacctgaaga	60
<400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgccca gcagtttgca gaaactgcgc acaagcttgc	catgaagcac aaatgttgag	120
<400> 317 CCTTGAATGA GCGTGGGAGAGGAGGAGGAGGAGGAGGGCCCA GCAGTTTGCA GAAACTGCGC ACAAGCTTGCAAACTGCCTA TCCTGGTGAACTGAA	catgaagcac aaatgttgag gagtttgttc agcagttttt	120 180
<400> 317 CCTTGAATGA GCGTGGGAGAGGAGGAGGAGGAGGAGGGCCCA GCAGTTTGCAAACTGCGC ACAAGCTTGCAAACTGCCTA TCCTGGTGAC TCTTCTTAAG AGAAACTGAAACAAGAATCCGAATCCAATCC	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt	120
<400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgccca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaatttttgttttt tcttttcaga tgttaatgtg aaagaaaggg	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc	120 180 240
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgttttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttctta ttaaaaaata	120 180 240 300 360 420
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgccca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgttttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttctta ttaaaaaata	120 180 240 300 360
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgttttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat ttttttgtag tttgaatatg aaatttggac caaatgataa</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttctta ttaaaaaata	120 180 240 300 360 420 480
<pre><400> 317 CCttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat tttttttgtag tttgaatatg aaatttggac caaatgataa <210> 318 <211> 340</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttctta ttaaaaaata	120 180 240 300 360 420 480
<pre><400> 317 Ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgttttt tctttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat tttttttgtag tttgaatatg aaatttggac caaatgataa gcaacatgta <210> 318</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttctta ttaaaaaata	120 180 240 300 360 420 480
<pre><400> 317 CCttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat tttttttgtag tttgaatatg aaatttggac caaatgataa <210> 318 <211> 340</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttctta ttaaaaaata	120 180 240 300 360 420 480
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgcta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat tttttttgtag tttgaatatg aaatttggac caaatgataa gcaacatgta <210> 318 <211> 340 <212> DNA <213> Homo sapien <400> 318</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttcttta ttaaaaaata actgcgctga gtctaaactg	120 180 240 300 360 420 480 490
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgcta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat ttttttgtag tttgaatatg aaatttggac caaatgataa gcaacatgta <210> 318 <211> 340 <212> DNA <213> Homo sapien <400> 318 cctggagtcc aataaccacc ccctcatacc acaccctgtg</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttcttta ttaaaaaata actgcgctga gtctaaactg catacaccag ccaagccttt	120 180 240 300 360 420 480 490
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgcta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat tttttttgtag tttgaatatg aaatttggac caaatgataa gcaacatgta <210> 318</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttcttta ttaaaaaata actgcgctga gtctaaactg catacaccag ccaagccttt tgggggttct gcagtctttg	120 180 240 300 360 420 480 490
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgcta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat ttttttgtag tttgaatatg aaatttggac caaatgataa gcaacatgta <210> 318</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttcttta ttaaaaaata actgcgctga gtctaaactg catacaccag ccaagccttt tgggggttct gcagtctttg agtgtaaacc ttgcctgcc	120 180 240 300 360 420 480 490
<pre><400> 317 Ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgccta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtarg ttttgaatat ttttgtag tttgaatatg aaatttggac caaatgataa gcaacatgta <210> 318</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttcttta ttaaaaaata actgcgctga gtctaaactg catacaccag ccaagccttt tgggggttct gcagtctttg agtgtaaacc ttgcctgcc aggcagcagc catcttggcc	120 180 240 300 360 420 480 490
<pre><400> 317 ccttgaatga gcgtggagag cgattaggcc gagcagagga acagcgcca gcagtttgca gaaactgcgc acaagcttgc aaactgcta tcctggtgac tcttcttaag agaaactgaa acaagaattc gggacctccg cttgcttctt tttttccaat ttttgtttt tcttttcaga tgttaatgtg aaagaaaggg ctaatgatct tgctaataaa tgctacaata gcatcggctt tcccactgtg tgtatgtgtg tatatgtatg ttttgaatat ttttttgtag tttgaatatg aaatttggac caaatgataa gcaacatgta <210> 318</pre>	catgaagcac aaatgttgag gagtttgttc agcagttttt atttggacac ttagagtggt tgttgcattt ttacatttcc cattttgggt ttttgcctcc gttttcttta ttaaaaaata actgcgctga gtctaaactg catacaccag ccaagccttt tgggggttct gcagtctttg agtgtaaacc ttgcctgcc aggcagcagc catcttggcc tctagccaga ggtgtagcct	120 180 240 300 360 420 480 490

```
<210> 319
      <211> 373
      <212> DNA
      <213> Homo sapien
      <400> 319
aaagatgctg ttaatgaaca ttacggacaa ttcatggtgt ggctagttgg taacacttca
                                                                        60
gctgattttt cttatgagat ggaaaaaaaa atcagccaag taagggcaca tcttcagttc
                                                                       120
atttagaagt cagcatccaa ggtaaaagaa ttctctgttg gacttgacat cactcccatc
                                                                       180
ctctgatact cgcctactct cttctcaaag aagttagtct ttccttccag tgaaatattc
                                                                       240
tocataaagt caaatgggtt ototactotg aaaacottgo taaaacccag ttocagcata
                                                                       300
agtotgtong coacaaacto aangtatigo thoattagag tgcaattcat gccaatgago
                                                                       3.60
                                                                       373
ttcacaggca agg
      <210> 320
      <211> 509
      <212> DNA
      <213> Homo sapien
      <400> 320
aaaaacaaaa ttaaatttto atttoaatta agaccoottt tggcattetg ottacttatt
                                                                        60
ctgccctttg gttaacagca tcagcatcac attactattt tatattgcat atatgtagca
                                                                       120
tttgcttcct taagttttca acatatcatt tatatttaaa ggcagacact gagtcagtat
                                                                       180
taatagatta actaaactgc actgtaattt agataaaatt actgtgtctc actgtgtatt
                                                                       240
acatgcaaaa tccacataaa ttgtcattta accaacagta ctgcacgagc gaacatctcg
                                                                       300
atatatgaaa actgcatcat caattcaacg ttttggtact tgaaactgca tcataaatgc
                                                                       360
aacattgtca tatgtgaaaa cgacacccta agtocttctt tttaaaaaatg acattgcgtt
                                                                       420
                                                                       480
tagettattg taagaggttg aacttttgta ttttgtaact atetttaage tetteagttt
                                                                       509
ataattcata taaaatgcct ttt.gtattt
      <210> 321
      <211> 617
      <212> DNA
      <213> Homo sapien
      <400> 321
                                                                        60
ccaaggcccc ttttgcagcc cacggctatg gtgccttcct gactctcagt atcctcgacc
                                                                        120
qatactacac accgactatc tcacgtgaga gggcagtgga actccttagg aaatgtctgg
aggageteca gaaacgette ateetgaate tgecaacett cagtgttega ateattgaca
                                                                        180
aaaatggcat ccatgacctg gataacattt ccttccccaa acagggctcc taacatcatg
                                                                        240
tectecetee caettgecag ggaacttttt tttgatggge teetttattt ttttetaete
                                                                        300
ttttcaggcg cactcttgat aaatggttaa ttcagaataa aggtgactat ggatataatt
                                                                        360
gagccctctg gtccaggtct cagtttacct aatattacct cagaaaggat atggagggaa
                                                                        420
gatgatettt ttgccaggte tgaettttet teetgeteeg eeeteeatta aegeteagta
                                                                        480
                                                                        540
ccctttagca gctgacggcc ccacgttcta ctccatgctt ggcttccttt ccaactagct
                                                                        600
ctttcatata ttttacttgc tagtatctcc attctctcta aagtagtggt tctttttgcc
                                                                        617
cttaaactta aattttt
       <210> 322
       <211> 403
       <212> DNA
       <213> Homo sapien
       <400> 322
```

```
aaaaagaagg acttagggtg tcgttttcac atatgacaat gttgcattta tgatgcagtt
                                                                        60
tcaagtacca aaacgttgaa ttgatgatgc agttttcata tatcgagatg ttcgctcgtg
                                                                       120
cagtactgtt ggttaaatga caatttatgt ggattttgca tgtaatacac agtgagacac
                                                                       180
agtaatttta totaaattac agtgcagttt agttaatota ttaatactga ctcagtgtct
                                                                       240
gcctttaaat ataaatgata tgttgaaaac ttaaggaagc aaatgctaca tatatgcaat
                                                                       300
ataaaatagt aatgtgatgc tgatgctgtt aaccaaaggg cagaataaat aagcaaaatg
                                                                       360
ccaaaagggg tcttaattga aatgaaaatt taattttgtt ttt.
                                                                       403
      <210> 323
      <211> 298
      <212> DNA
      <213> Homo sapien
      <400> 323
ccagaattag ggaatcagaa tcaaaccagt gtaaggcagt gctggctgcc attgcctggt
                                                                        60
cacattgaaa ttggtggctt cattctagat gtagcttgtg cagatgtagc aggaaaatag
                                                                       120
gaaaacctac catctcagtg agcaccagct gcctcccaaa ggaggggcag ccgtqcttat
                                                                       180
atttttatgg ttacaatggc acaaaattat tatcaaccta actaaaacat tccttttctc
                                                                       240
ttttttcctg aattatcatg gagttttcta attctctctt ttggaatgta gattttt
                                                                       298
      <210> 324
      <211> 78
      <212> DNA
      <213> Homo sapien
      <400> 324
ccatgggaag gtttaccagt agaateettg ctaggttgat gtgggccata catteettta
                                                                        60
ataaaccatt gtgtacat
                                                                        78
      <210> 325
      <211> 174
      <212> DNA
      <213> Homo sapien
      <400> 325
ccatcatggt caggaactcc gggaagtcaa tggtcccgtt cccatctgca tccacctcat
                                                                       60
tgatcatate etgeagetet getteagtgg ggttetgtee eagggatete ateactgtee
                                                                       120
ccaactcctt ggtggtgata gtgccatctc catccttgtc aaagagggag aagg
                                                                       174
      <210> 326
      <211> 679
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(679)
      \langle 223 \rangle n = A,T,C or G
      <400> 326
aaaactgaaa tacctcttaa aataatttga tccccagcgt ttgctctttt tgaagtaacc
                                                                        60
aacttactct taaaaaggat ggntgccaag atggaaagtc ttactgggtt ttcatgttaa
                                                                       120
cctattcttt ggacataact atgaattttg tatacaatgc acttcatgaa aagttgtggc
                                                                       180
tcccccagat tgcccacaag tgtgatcttg aagtcctaaa catttgtcca tgtaaqcttc
                                                                       240
aaaacagcgt taactgagtt attcaagtag cagtacttaa agatacaatt cttgaagcag
                                                                       300
```

WO 00/37643 PCT/US99/30909

100

```
tttcaatggt ttctgatcca aataatcagt ttctgaacat tactacttca cataatagag
                                                                        360
tccatcttca gtttcttctc actttctctt tcccttttgg gtttcctttt tgtggcctga
                                                                        420
ggccaccagt tctttgggta ctatcaagat acttccatca tgggtacact ggagagcata
                                                                        480
gtggttggga ttgactggcc taccttggtc atctcttaat ctactaaaaa tatcatqata
                                                                        540
aaggtcatgc agtttctgtt tcattatgtt aatagctttg gtacattgtg cttgctctt
                                                                        600
cttaanagtt tccttctttg cttgcaagtt acatacatca tcttctaaat tcaaaattat
                                                                        660
gtccattttg gcgtttacc
                                                                        679
      <210> 327
      <211> 619
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(619)
      <223> n = A,T,C \text{ or } G
      <400> 327
aaaataagtt actggtaaat ggagttgcat tctatagtca cttaataaat attaacaaaa
                                                                        60
tatttataac tggaacctta atgaaatgta tcatcaaatc aggtaaaagc aacttgtccg
                                                                       120
cagttaccaa agcctanata cgcgttagat gcgccttttc cggcctgtgc gtctgctctg
                                                                       180
gttcctctca ggcagcaaag ctggggaagg aagctcaggc aggagcctcc ccgacgccac
                                                                       240
aacggcacaa gcagcagcta aagcaccgca ctttgctcta ctaacctttt acttaaatga
                                                                       300
ggttttgcca aatccacatc tgyaaccgcg tcacacccat ttgcaaggat gtttgttctt
                                                                       360
tgatgaaact gcatctctac tgcacatgag ggctttcatt gtaggacaag aggagagttc
                                                                       420
gtttattttt gtaactgttt tacatgttcc gattagttaa tcggtagctt atgtcatttg
                                                                       480
ctatgcctgn agnettetaa teteteetta etaaaacatt aetteaaatt tgaattgace
                                                                       540
cttggttata atttatttag ccgggatttg tgtgtcattg tagagcaact ctaattcaag
                                                                       600
aatagtgaca acttttaag
                                                                       619
      <210> 328
      <211> 132
      <212> DNA
      <213> Homo sapien
      <400> 328
aaatccaaat acaaaagcat agtctctgca agattttgtt ctttgaattt cttgatattg
                                                                        60
taattgatta ttgataactg tcatcatgaa attatctctc aataataaga taaataaact
                                                                       120
agcatatgaa tc
                                                                       132
      <210> 329
      <211> 854
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(854)
      <223> n = A, T, C or G
      <400> 329
ccttgaggta actattgcaa aatatacagt gtaagttcag tctgatggaa accccagatt
                                                                        60
catcaaggat acaaatctac agtagcccaa tggcggtttc atagtgtata atttattatc
                                                                       120
aataaaatta actccgttac aatcagcatt catttcctcc aattaaaatt aagcataaac
```

cctaggtagt aaccttctgc gcaaaaacaa tattcaagct tatacaatag acaagacagg aaggtggaga aaatgatgaa cactgggaaa ttcttacagc acatattcca ctacagagct agttcaaatt gaattctatc tttgaatcac aaaacataat aatctgccgc acaaactgca catcacagtt gtgcattata gggtaggatt ttttaccctc natattccnt tcac	tgtctgatta actatataga tctatgcatc tactttacaa atactctatg ttccacaatc taccacaata aattaaatta	tgcatatttt taatggacag cccgagaaca tcataggtta caactgtttt acaatgggtg aaacacagtg actacacaga tttctttcct	ctttaatcat acttaaatgc cttaaaattt acagcctagt ttcccctcat catcacccag ttcaagtatc ctaaaaacta ttggttttaa	atagattata ccgcattttt tttttattt tatacagaag aaacaacctg tacacagaag ttggcagagc tacagcctac gtcaggaaca	240 300 360 420 480 540 600 660 720 780 840 854
<210> 330 <211> 299 <212> DNA <213> Homo sapie	en				·
<pre><400> 330 ccaatgaata actgacttta ctcgacactt ttcactcatg tgccctcacc agcttgtgta ataaatgccg gtctaagtga tcttgcagag ttcagaaact <210> 331</pre>	gattetteaa tttteacaaa aagteateeg	atttatggtt aacgctcccg atgacagctc	aaagaggcac atcatctcgg agccacccgg	ttatacactc caagcaaaat agaatggctt	60 120 180 240 299
<211> 573 <212> DNA <213> Homo sapio	en				
aaagatatga acagcttaat agcaaaatgt tcaagttaaa catgaaaaca aatggtctgt gaaaatttaa tatcttctca aaggaactta tgtaatgtaa	aaaaaaacat aatcttataa aacaggcata aattacatta ttgactgcaa cttttctgta tttccctccc caaaaaaatt	accgggtgag accaacatag agatgaagaa taatttttca atagtaatgc gttgacatat caagaaaatg ctgatttata	caatgcacta catttcactg gtgctatttt ttccgaattg aatataattt gaagaccact tctcacaatt	aaattatcca tcaacaatgt ttaattgtaa acaaatgatt cataaaaatc tcaatttcta acaaagtaga	60 120 180 240 300 360 420 480 540 573
<210> 332 <211> 555 <212> DNA <213> Home sapid	en				
<pre><400> 332 aaatttgaaa gttgtaagca tgtccttttc tggttgcctc agtaagttat agacttgctg caaaacttca gaatattagc taaaattttt gaaatcacta ctctgtgtaa ctggttacat attagaaaat acatacctat</pre>	tctatgctat agtttggcat atattaccac ctgttacctg tttgatggtt	tgtgttcaga agatagtgcg aaataatttt ttatagaaaa gtctatactc	tacttacacc ctcatttaat tggtgaaact tagtgttggc aactggatat	ataattaaac ctgtgcctct attgagatat ttagtctagt gtgtatgtaa	60 120 180 240 300 360 420

```
ctacataatt tgtagctcat catttttcct taatcctttc ctaacttgtc gcagcagttt
                                                                        480
gaatttccca gatatttatg tttgaacata atggctcaga atacatattt gaacatcata
                                                                        540
gttgtatata ttttt
                                                                        555
      <210> 333
      <211> 460
      <212> DNA
      <213> Homo sapien
      <400> 333
aaatttettt caacagteta ttggggteea aaaageatat atcaaaacaa aaataacaaa
                                                                        60
agcaaaacaa aatgctacat gtaaaagcta aagaaagaaa atgcagcata ttcaggttct
                                                                       120
ttttcttgag gtacctatat aaatttaatc acctgcccca aagtcctctc gttaggttaa
                                                                       180
aaacacaatg cgtcctgggg agccaattgc ccggcacgtc ttattactga gaaagtgcaa
                                                                       240
gaatgctgat catcttatgc agcatactaa aggatgattt actctttaca aaatagagct
                                                                       300
taagtatcaa cctgatggaa gttagaaaat taaaaaacatt taagtagaat catctctctc
                                                                       360
totatttttg agatootgca gcaaaaagco toccaaatca actttcaaag ttotgccatt
                                                                       420
aaggaatgtt ggttctcttg taaaattcag agatctcttt
                                                                       460
      <210> 334
      <211> 190
      <212> DNA
      <213> Homo sapien
      <400> 334
ccaaggaagg ctgtgctcta gcccatctga ccctgtctgc aaaccacctg ggggacaagg
                                                                        60
ctgatagaga cctgtgcaga tgtctctctc tgtgcccctc actcatctca ctggatctgt
                                                                       120
ctgccaaccc tgagatcagc tgtgccagct tggaagagct cctgtccacc ctccaaaagc
                                                                       180
ggccccaagg
                                                                       190
      <210> 335
      <211> 394
      <212> DNA
      <213> Homo sapien
      <400> 335
aaatttggac agacttctag cggacagtta cttctcaaga attttctata caaaagctgt
                                                                        60
gccaggcata tattttctca ccaggacaca tggggcagcg gacccctggt gtcagtaaga
                                                                       120
acacacccag aatgatataa ccagatattt ttcagtttct aaattaaggc atattcaaaa
                                                                       180
aattccatgt acaagtttac accacttttc taagttactc accaggtaat taaagcagat
                                                                       240
tcacagatga attactctca gtttaactat atgcaacaac catgccaata acttttcttc
                                                                       300
taaattttgc ataataatgg ttaaaaaaag tggtagttta actatcatgt tcacaattgt
                                                                       360
catttttcaa ggcagtagaa gaccaagaca tttt
                                                                       394
      <210> 336
      <211> 429
      <212> DNA
      <213> Homo sapien
      <400> 336
aaaagctatc accattgtag tagaatcatc cttcttttt gaaatttgaa gcatcccagg
                                                                       60
cttaaaatct tgtgtttcag aaagacagtt tataccatga ctgcttaatt atcccccaa
                                                                       120
agaccttctg attgaagtca tgtacagttc agtggcctaa attctctgcc tttttaactt
                                                                      180
gctttgcaag cctactctga aaataagtta tttagtcaag ttattctcaa agatgtccca
                                                                      240
gttgcctaga aaggatcaaa tggaacattt gacacacata ctcaaaaaaa tgtaactgac
                                                                      300
```

```
tataaacact ttaacctaat catctgtatc aaactttcta aaaatcaaat ctcaggattg
                                                                     360
ttccacttta gagattctat gtaaagttta tataactata cttgtcaaat agcacctatc
                                                                     420
tatqcattt
                                                                     429
      <210> 337
      <211> 373
      <212> DNA
     <213> Homo sapien
      <400> 337
aaagatgctg ttaatgaaca ttacggacaa ttcatggtgt ggctagttgg taacacttca
                                                                     60
gctgattttt cttatgagat ggaaaaaaaa atcagccaag taagggcaca tcttcagttc
                                                                     120
atttagaagt cagcatccaa ggtaaaagaa ttctctgttg gacttgacat cactcccatc
                                                                     180
ctctgatact cgcctactct cttcccaaag aagttagtct ttccttccag tgaaatattc
                                                                     240
tccataaagt caaatgggtt ctctactctg aaaaccttgc taaaacccag ttccagcata
                                                                     300
agtotgtotg coacaaacto aatgtattgo ttoatcagag tgcaattcat cocaatgagt
                                                                     360
ttcacaggca agg
                                                                     373
      <210> 338
      <211> 366
      <212> DNA
     <213> Homo sapien
      <400> 338
ccatcccctt atgagcgggc gcagtgatta taggctttcg ctctaagatt aaaaatgccc
                                                                      60
tagcccactt cttaccacaa ggcacaccta caccccttat ccccatacta gttattatcg
                                                                     120
aaaccatcag cctactcatt caaccaatag ccctggccgt acgcctaacc gctaacatta
                                                                     180
ctgcaggcca cctactcatg cacctaattg gaagcgccac cctagcaata tcaaccatta
                                                                     240
accttecete tacaettate atetteacaa ttetaattet actgaetate etagaaateg
                                                                     300
ctgtcgcctt aatccaagcc tacgttttca cacttctagt aagcctctac ctgcacgaca
                                                                     360
acacat
                                                                     366
     <210> 339
      <211> 319
      <212> DNA
     <213> Homo sapien
      <400> 339
60
caacacagta tgtctggggc tagatttcaa aacccacgta atgaaaaagt cagttttaca
                                                                     120
agcctaattt tgttgttttt ttttttatat caattaacgt taaaaattgc atcaactatt
                                                                     180
taattcatga ggatctttca tattaaaatt taaccttaag attcaaccgc catgtgcttt
                                                                     240
tataaaggaa acatttttta gagacgtctg agctcacttt tacatggtgg tgcctactgc
                                                                     300
cgttaatgtt tgtgatttt
                                                                     319
      <210> 340
      <211> 278
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
     <222> (1)...(278)
      \langle 223 \rangle n = A,T,C or G
```

```
<400> 340
ctaataaaat gaattaacca ctcattcatn natctaccca cccnatccaa catctccnca
                                                                      . 60
tgatgaaacn ncggctcact ccttggcgcc tgcctgatcc tccaantcac cacaggacta
                                                                       120
ttcctagcca tgcactactn accagacnec tcaacngcct tttnatcaat nggncacatn
                                                                       180
actoganach taaatnatgg otgaatoato ogotacotho acgocaatgg cagootcaat
                                                                       240
attetttatg etgeetette etacacatge gggegagg
                                                                       278
      <210> 341
      <211> 400
      <212> DNA
      <213> Homo sapien
      <400> 341
ccagcatggg gctgcagctg aacctcacct atgagaggaa ggacaacacg acqqtqacaa
                                                                       60
ggetteteaa cateaaceee aacaagaeet eggeeagegg gagetgegge geeeacetgg
                                                                       120
tgactctgga gctgcacagc gagggcacca ccgtcctgct cttccagttc gggatgaatg
                                                                       180
caagttctag ccggtttttc ctacaaggaa ttcagttgaa tacaattctt cctgacgcca
                                                                       240
gagaccetge etttaaaget gecaaegget eeetgegage getgeaggee acagteggea
                                                                       300
attectacaa gtgcaacgeg gaggagcacg teegtgteac gaaggegttt teagtcaata.
                                                                      360
tattcaaagt gtgggtccag gctttcaagg tggaaggtgg
                                                                       400
      <210> 342
      <211> 536
      <212> DNA
      <213> Homo sapien
      <400> 342
aaagaacaat gggaaaaaca agtccgtgtt ctcacagatg ctgtcgatga cattacttcc
                                                                       60
attgatgact tcttggctgt ctcagagaat cacattttgq aagatgtgaa caaatgtgtc
                                                                      120
attgctctcc aagagaagga tgtggatggc ctggaccgca cagctggtgc aattcgaggc
                                                                      180
egggeageec gggteattea egtagteace teagagatgg acaactatga geeaggagte
                                                                      240
tacacagaga aggttctgga agccactaag ctgctctcca acacagtcat gccacgtttt
                                                                      300
actgagcaag tagaagcagc cgtggaagcc ctcagctcgg accctgccca gcccatggat
                                                                      360
gagaatgagt ttatcgatgc ttcccgcctg gtatatgatg gcatccggga catcaggaaa
                                                                      420
gcagtgctga tgataaggac ccctgaggag ttggatgact ctgactttga gacagaagat
                                                                      480
tttgatgtca gaagcaggac gagcgtccag acagaagacg atcagctgat agctgg
                                                                      536
      <210> 343
      <211> 646
      <212> DNA
      <213> Homo sapien
      <400> 343
aaaacttcta ttcatcaaaa gacataaaga aaacagtcaa gccacagact aggtgtaata
                                                                       60
totcaataca tatatoogac aagagaattg catotagaat gtataaagaa tttotatqac
                                                                      120
ccaattatag ctatcaggga tatacaaatt aaaaccaaaa tgaaacatca ctacacaccq
                                                                      180
attggaatgg ttaaaaagga aaaatactga caacaccaat atttgtaaaq acaqqaqqta
                                                                      240
ccagaactct cattcattat attcataaat tgacaaatat aaaaactgct atagtagggc
                                                                      300
agtcttcctt agaaagggat tgtgggcatg acagagaaca atattaatct gtccattata
                                                                      360
ttccttaact gtaaaatgga gaccatatgt tccaccagct tcacttggta attatgatac
                                                                      420
atggctatta agagactcaa atgactccat ttcatcaact aatatgccct qtcaattcta
                                                                      480
cttctaaagt atcccatgtt ctatccaatg tcataccact atcataattt aagtgttcat
                                                                      540
aactctctat aatatttcaa taatctaact ggtctcaatg cctgtagtag aaattgcaga
                                                                      600
ttgggctccc caatttctgt tccctaggaa ggctgagaaa gctttt
                                                                      646
```

<210> 344 <211> 383 <212> DNA <213> Homo sapien <400> 344 cctgcacccc agtataaggg cctccccage tgagtaagaa gctgcttccc ctcctctat 60 aggccaagcc tattgtgtga aaccatctca tggtcttggt gacgtagacc atttttgaaa 120 ccgtctcatg gtcttggtga cgtagaccgt ttgcttcttt aactccagcc gcggaatgac 180 attagtggaa ccgygctagg gaactgctgg aagttcagga tgccaccacc ttgaacacct 240 aggecaggga tececaceat gtecegggtt tetttetteg agagtataga accqtteatt 300 cttgctttgt gtcccattcc atctcttgaa aaaatgtagt ctttgaatgt gtgaaaatct 360 agggacattc aatctagtct ttt 383 <210> 345 <211> 263 <212> DNA <213> Homo sapien <400> 345 ceteccette ceetttgetg gtgggaggag etegtgtget cettggeege ttactggaag 60 ggcgtttttc agagctgcag ggacagggtg agcagctgaa gggctaggag ggaagccggc 120 edecegetetg cagaagetge attteagetg aatetgtgtt teageeteag ttggttgeae 180 cgttagcccc tetecteccg gatggteatg tttttgteac attagagaat aaacagccac 240 acacacattt tttttttcc ttt 263 <210> 346 <211> 132 <212> DNA <213> Homo sapien <400> 346 aaatccaaat acaaaagcat agtctctgca agattttgtt ctttgaattt cttgatattg 60 taattgatta ttgataactg tcatcatgaa attatctctc aataataaga taaataaact 12.0 agcatatgaa to 132 <210> 347 <211> 564 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(564) <223> n = A, T, C or G<400> 347 cctgggtatc cagggaggct ctgcagccct gctgaagggc cctaactaga gttctagagt 60 ttctgattct gtttctcagt agtcctttta gaggcttgct atacttggtc tgcttcaagg 120 aggtcgacct tctaatgtat gaagaatggg atgcatttga tctcaagacc aaagacagat 180 gtcagtgggc tgctctggcc ctggtgtgca cggctgtggc agctgttgat gccagtgtcc 240 tctaactcat gctgtccttg tgattaaaca cctctatctc ccttgggaat aagcacatac 300 aggettaage tetaagatag ataggtgttt gteettttae categageta etteecataa 360 taaccacttt gcatccaaca ctcttcaccc acctcccata cgcaagggga tgtggatact 420 tggcccaaag taactggtgg taggaatett agaaacaaga ccaettatae tgtetgtetg 480

```
aggnagaaga taacagcagc atctcgacca gcctctgcct taaaggaaat ctttattaat
                                                                        540
 cacgtatggt tcacaagata attc
                                                                        564
       <210> 348
       <211> 321
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(321)
       <223> n = A,T,C or G
       <400> 348
geneatgaac anggageaac ganaagagar gteegggetaa gggeegggga cgggcgc
                                                                         60
ccatcctgcn acggaacacn ttcgggttnt ggttttgatt ngttcacctc tgtttatatg
                                                                        120
canctatttg ntcctcctcc cccaccccag nccccaactt catgcttntc ttccgcnctc
                                                                        180
ageenceetg ecetgteete geggtgagte antgaceaen gntteecetg cangageege
                                                                        240
egggegtgag aenengacee tenntgeata caccaggeeg ggeeennget ggeteeceen
                                                                        300
gnggccctgt gaaanagctg g
                                                                        321
       <210> 349
       <211> 255
       <212> DNA
       <213> Homo sapien
       <400> 349
ccatgacagt gaaggggctg ttaggaatat caacaccacc gaagcgcaca tagatcacat.
                                                                        60
atgtgcccgg cttggcagct gtgtagaaga tgtcataggt tccatcttca ttctcaatga
                                                                       120
categgeete ggeeteagtg ceatetgggg teagaacegt geaggteact ttaccettee
                                                                       180
cggcagtctt ggcatcaacc acaaagccta cttcttcgcc agttttcaca gtggaggcga
                                                                       240
ttccaggacc cgtag
                                                                       255
      <210> 350
      <211> 496
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(496)
      <223> n = A, T, C or G
      <400> 350
gggcttattn gctcacaaaa tcattcnctt ttggaactat ggccaattga agctacacac
                                                                        60
tgaatttatt aatacagcat taagtttctt tgtgtnaaaa aatctttgtn cncagtaata
                                                                       120
aaaaaagata aggcaagatg cattaaacat gaaaccttct ggctcttttc ctctgcgttt
                                                                       180
ttacagagcc actgatgact atctgcaaca aaagagttaa gtttctgatt ttccgtatca
                                                                       240
agcatcttat gcctttgctg tggtaagaat tctggccaag caccctgaag gacagatgct
                                                                       300
ggtgatggnc tttggcactt atgctggcaa actgagcttc tttcccttga gtacttttgn
                                                                       360
aatgtacaag tagaagaagt cacaagtata ggatggtctg gactacgccg gccaccacag
                                                                       420
caatgaggtc aaagaagccc tcaaagnaga agcgnccaga tccagttgac aagatacaaa
                                                                       480
gcacgataga ggccca
                                                                       496
      <210> 351
```

```
<211> 109
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(109)
      <223> n = A, T, C \text{ or } G
      <400> 351
ccatagtgaa gcctgggaat gagtgttact gcagcatctg ggctgccanc cacagggaag
                                                                        ,60
ggccaagccc catgtagccc cagtcatcct gcccagcccc gcctcctgg
                                                                        109
      <210> 352
      <211> 384
      <212> DNA
      <213> Homo sapien
      <400> 352
ccttcgagag tgacctggct gcccaccagg accgtgtgga gcagattgcc gccatcgcac
                                                                        60
aggageteaa tgagetggae tattatgaet eacceagtgt caaegeeegt tgecaaaaga
                                                                        120
tctgtgacca gtgggacaat ctgggggccc taactcagaa gcgaagggaa gctctggagc
                                                                       180
ggaccgagaa actgctggag accattgacc agctgtactt ggagtatgcc aagcgggctg
                                                                       240
caccetteaa caactggatg gagggggeea tggaggacet geaggaeace tteattgtge
                                                                       300
acaccattga ggagatccag ggactgacca cagcccatga gcagttcaag gccacctcc
                                                                       360
ctgatgccga caaggagcgc ctgg
                                                                       384
      <210> 353
      <211> 345
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(345)
      <223> n = A, T, C or G
      <400> 353
ccttggtcag gatgaagtng gctgacacac cttagcttgg ntttgcttat tcaaaagana
                                                                        60
aaataactac acatggaaat gaaactagct gaagcctttt cttgttttan caactgaaaa
                                                                       120
ttgnacttgg ncacttttgt gcttgaggag gcccattttc tgcctggcag ggggcaggta
                                                                       180
tgtgccctcc cgctgactcc tgctgtgtcc tgaggtgcat ttcctgttgn ncacacaang
                                                                       240
gccangntcc attctccctc ccttttcacc agngccacan cctnntctgg aaaaangacc
                                                                       300
agnggtcccg gaggaaccca tttgngctct gcttggacag canag
                                                                       345
      <210> 354
      <211> 712
      <212> DNA
      <213> Homo sapien
      <400> 354
ccatctacaa tagcatcaat ggtgccatca cccagttctc ttgcaacatc tcccacctca
                                                                       60
gcagcetgat egeteageta gaagagaage agcageagee caccagggag etectgeagg
                                                                       120
acattgggga cacattgagc agggctgaaa gaatcaggat tcctgaacct tggatcacac
                                                                       180
ctccagattt gcaagagaaa atccacattt ttgcccaaaa atgtctattt ttgacggaga.
                                                                       240
```

```
gtctaaagca gttcacagaa aaaatgcagt cagatatgga gaaaatccaa gaattaagag
                                                                                                                                            300
 aggeteagtt atacteagtg gaegtgaete tggaeceaga caeggeetae eccageetga
                                                                                                                                            360
 tcctctctga taatctgcgg caagtgcggt acagttacct ccaacaggac ctgcctgaca
                                                                                                                                            420
 accccgagag gttcaatctg tttccctgtg tcttgggctc tccatgcttc atcgccggga
                                                                                                                                            480
 gacattattg ggaggtagag gtgggagata aagccaagtg gaccataggt gtctgtgaag
                                                                                                                                            540
 actcagtgtg cagaaaaggt ggagtaacct cagcccccca gaatggattc tgggcagtgt
                                                                                                                                           600
 ctttgtggta tgggaaagaa tattgggctc ttacctccca atgactgccc tacccctgcg
                                                                                                                                           660
 gaccccgctc cagcgggtgg gggattttct tggactatga tgctggggga gg
                                                                                                                                            712
            <210> 355
            <211> 385
            <212> DNA
            <213> Homo sapien
\sim in the distribution of the properties of th
 cctcatagee gettageaca gttacagaat gtetgaaggg gacagtgtgg gagaateegt
                                                                                                                                             60
ccatgggaaa ccttcggtgg tgtacagatt tttcacaaga cttggacaga tttatcagtc
                                                                                                                                           120
ctggctagac aagtccacac cctacacggc tgtgcgatgg gtcgtgacac tgggcctgag
                                                                                                                                           180
ctttgtctac atgattcgag tttacctgct gcagggttgg tacattgtga cctatgcctt
                                                                                                                                           240
ggggatctac catctaaatc ttttcatagc ttttctttct cccaaagtgg atccttcctt
                                                                                                                                           300
aatggaagac ccagatgacg gtccttcgct acccaccaaa cagaacgagg aattccgccc
                                                                                                                                           360
cttcattcga aggctcccag aqttt
                                                                                                                                           385
            <210> 356
            <211> 347
            <212> DNA
            <213> Homo sapien
            <400> 356
aaatgagata aagaaagtot oottitigitt tiagatggaa aagaaagoac aagtittiito
                                                                                                                                            60
tacctgrgaa tgaactttgg tgacctatat gtgccattca tgcagcattt ttgttcatat
                                                                                                                                          120
tggcttagaa ttcagtgcat gaatatcatt acattcttat atctaacatt cctagttagc
                                                                                                                                          180
tttgattcaa aatatacaaa atctgataca tgaatacttt gctagattaa tgacttgatc
                                                                                                                                          240
atctttggaa tgagtaggca agacgatttt tacctattat ttctatgttg tgggtaatgt
                                                                                                                                          300
taaaactaaa tacagatgat aataattgct atttcacagt gatgttt
                                                                                                                                          347
            <210> 357
            <211> 313
            <212> DNA
            <213> Homo sapien
            <400> 357
aaagtaatca acctctctgt ccttccatta gtctggatcg tctaaagatt gttttatttt
                                                                                                                                            60
tagaggetea teeggteaga tgttagtgat gtgaaattte aggeeaggeg tgaeqteage
                                                                                                                                          120
gtggcatttg aaacagctcc atgttgccct tagtgctgtc tgaccgaagc ctgtctgtcc
                                                                                                                                          180
tcagatataa agatgaagcg cagctgtata aagaagagca cctgaggaat cggcagcacc
                                                                                                                                          240
ctcactgcta cgttcagtac atgatcgcca tcatcaacaa ctgccagacc ttcaaggaat
                                                                                                                                          300
ccatagtcag ttt
                                                                                                                                          313
            <210> 358
            <211> 403
            <212> DNA
           <213> Homo sapien
           <400> 358
```

```
aaaaagaagg acttagggtg tcgttttcac atatgacaat gttgcattta tgatgcagtt
                                                                          60
 tcaagtacca aaacgttgaa ttgatgatgc agttttcata tatcgagatg ttcgctcgtg
                                                                         120
 cagtactgtt ggttaaatga caatttatgt ggattttgca tgtaatacac agtgagacac
                                                                         180
 agtaatttta totaaattac agtgcagttt agttaatota ttaatactga otcagtgtot
                                                                         240
 gcctttaaat ataaatgata tgttgaaaac ttaaggaagc aaatgctaca tatatgcaat
                                                                         300
 ataaaatagt aatgtgatgc tgatgctgtt aaccaaaggg cagaataaat aagcaaaatg
                                                                         360
 ccaaaagggg tcttaattga aatgaaaatt taattttgtt ttt
                                                                         403
       <210> 359
       <211> 411
       <212> DNA
       <213> Homo sapien
       <400> 359
 aaataaatac ttagaacacg acttggctcc tacaagcatc tggactctag gtctcagtac
                                                                         60
tggagtgtct cacccatggg ccccacgcag ggacgccacg gttccctccc accccqtqat
                                                                        120
caagacacgg aatcggctgc cgatggttgg atcgcaatgc gccccttttc tagagccttc
                                                                        18.0
cccggccatc tacaggcagg atgcggctgg gaaaaagaca actggaattt ctcgaaggtt
                                                                        240
gatggtccgc acggttgagg attctacgtg gttctcttgg ttcccctggt gtgtgtgt
                                                                        300
gtggaggagg ccgcggccct tagatcacct tcttgagctc gtcgtacagg accaqcacqa
                                                                        360
aggegeéece catgeecege aggaegttgg accaegeace ettgaagaag g
                                                                        411
       <210> 360
       <21.1> 378
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(378)
       <223> n = A, T, C \text{ or } G
       <400> 360
cctcttcagg ggcccgagcc agggacaggg ccttggtttc cttctccctg gcttctgcct
                                                                         60
cagctetgte ecteteatee gegtatttgg aagagatgtt ttteteeteg getaacaact
                                                                        120
gatcaaattt cctctgcttc ttttccaggt tggacacgag ttgccgctgg ttgtccaaat
180caacaaccag gtcgtccagc tcctgctgaa gcctgttctt ggtcttttcc agtttatcat
aageggeege etteteeteg taetgetggg tgaggntete gateteette tggaacetet
                                                                        300
tettececte ttecagaget tecaeggnge tggcaaagte etgeagette ttettegagt
                                                                        360
cggagagctg gatgttga
                                                                        378
       <210> 361
       <211> 372
       <212> DNA
       <213> Homo sapien
       <400> 361
aaatactggg ggccattaag agtggatgta gctaagagct tagctaacat tgccttttca
                                                                         60
ctctattttt ctcagatatt gtaagcattc tgtttttcaa tattgtagtt aattttttgg
                                                                        120
etttcaacag cagecetagt aatggtggag ttgttaatta atgtgtatat tgtactgaat
                                                                        180
ttctgtcagt taaggggttc actgctttgg tggaaattgg tggaaattgc tagcaggttc
                                                                        240
cacgatgttt attitttct ccatgttgta tatcattacc atticacata cgcgtttcta
                                                                        300
tttttcttcc tctcctcctg atctccttaa aaatgaatct agagttggtg gctttttccc
                                                                        360
cctcctcttt gg
                                                                        372
```

```
<210> 362
       <211> 544
       <212> DNA
       <213> Homo sapien
       <400> 362
 cctgagtcac ctagcatagg gttgcagcaa gccctggatt cagagtgtta aacagaggct
                                                                         60
 tgccctcttc aggacaacag ttccaattcc aaggagccta cctgaggtcc ctactctcac
                                                                        120
 tggggtcccc aggatgaaaa cgacaatgtg cctttttatt attatttatt tggtggtcct
                                                                        180
 gtgttattta agagatcaaa tgtataacca cctagctctt ttcacctgac ttagtaataa
                                                                        240
 ctcatactaa ctggtttgga tgcctgggtt gtgacttcta ctgaccgcta gataaacgtg
                                                                        300
 tgcctgtccc ccaggtggtg ggaataattt acaatctgtc caaccagaaa agaatgtgtg
                                                                        360
 tgtttgagca gcattgacac atatctactt tgataagaga cttcctgatt ctctaggtcg
                                                                        420
gttcgtggtt atcccattgt ggaaattcat cttgaatccc attgtcctat agtcctagca
                                                                        480
 ataagagaaa tttcctcaag tttccatgtg cggttctcct agctgcagca atactttgac
                                                                        540
 attt
                                                                        544
       <210> 363
       <211> 328
       <212> DNA
       <213> Homo sapien
       <400> 363
aaactggtta tgacaaaagc ctttagttgt gtttcttgaa ctataaagaa aacaaatttt
                                                                        60
ggcagtcttt aagtatatat agcttaasat ataattttta gcatttggca ccatatgtat
                                                                       120
gecattatat tigattitge attactytti cacaatgaag ettiettiaa ggettigatt
                                                                       180
tttatgatta tgaaagaaat aaggcacaac cacagttttt ctttcttaaa tttcatcact
                                                                       240
gttgatgtgg ttcttttgtg ttaaaaaaaa aaagtgcaac tatcaaaact aaaaaattat
                                                                       300.
agagtaatat tgccgttctg ctgatttt
                                                                       328
      <210> 364
      <211> 569
      <212> DNA
      <213> Homo sapien
      <400> 364
cctgggcacc tctttgcttg aaatatggca agacttggaa aaatgtttgc ccttagaatc
                                                                        60
tatctcacta ctttagttag ttgtctcctt tgggcctggg cacagttctg gccctgatct
                                                                       120
ggaacagact cccttttcta aaactgaact tgaccacatc aaaagtttgt aaaacaatct
                                                                       180
ccatggtaat taaacttgca ttcaacacca tatggtaaca gaagatggca aaggataaga
                                                                       240
ttcagatctt agatctttcc aagtagggca tgttagatga tagaaggatt agttgcaagc
                                                                       300
tggatctgag ctcaggcttg ggcatgaagg aaactgtctc ccatgtggtt tggaagagtt
                                                                       360
aggggetece tgagetetat tgtgaactat acgggtttea tecaaggaat ggtatgatgt
                                                                       420
gggcataaaa ccattcttca gacaactgaa gatggtcccc ttctgtagcc agaaacacta
                                                                       480
gctgtcctgc attgtccatt tcctttagcc ccaggcggtc ctgtgtgtac agggaggtct
                                                                       540
cctgtaaggg aatggtttcc ttggcttgg
                                                                       569
      <210> 365
      <211> 151
      <212> DNA
      <213> Homo sapien
      <400> 365
aaaaaaaaaa atccttttat tatggaattt gtcaaacaca cacacaagca taacaaaccc
                                                                        60
```

PCT/US99/30909

111

WO 00/37643

```
ctaggtaccc atctccaagt tttgacccct attataattt catcttcagt gttttattat
                                                                       120
ccacttcctc tctctctatc tttagtattt t
                                                                       151
      <210> 366
      <211> 508
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(508)
      <223> n = A,T,C or C
      <400> 366
agtataaaga tatattooat aaaagagttt gycagtcaaa ganaagcatc ycacttooga
                                                                        60
aaaacacaaq cattcttctc ctaqtctaca qaqaattqnq taaaaaaaaaa aaaaaatcat
                                                                       120
catcaacago enccantnta enccacacta gaargtacae teeggeaagt aaattaaggn
                                                                       180
tgcagtccat ccctgaacga tganaagngg tctgagctat ggcaaagngt tanaaagtag
                                                                       240
cccagctana caaatgcccc agctatcccc aggggagtta ttcagtactt aanacttcat
                                                                       300
ttccaananc agccccggaa aagccctgac aggaaggggg gaccagngat caccgatntc
                                                                       360
ccattagggg cggncaccaa aaacaaaatg cctggagctt ntgagcagct gcagcctggg
                                                                       420
gttgtggcta ggcncngggn gnggttgcaa aaaaacqgct gtntccgggg agaggcaaat
                                                                       480
ggcaggccag ccagccctgg gtacatgg
                                                                       508
      <210> 367
      <211> 382
      <212> DNA
      <213> Homo sapien
      <400> 367
cctgagcggc tagtctttaa gatgcgcttc tatcgtttgc tgcaaatccg agcagaagcc
                                                                        60
ctcctggcgg caggcagcca tgtgatcatt ctgggtgacc tgaatacagc ccaccgcccc
                                                                       120
attgaccact gggatgcagt caacctggaa tgctttgaag aggacccagg gcgcaagtgg
                                                                       180
atggacaget tgeteagtaa ettggggtge eagtetgeet eteatgtagg geeetteate
                                                                       240
gatagetace getgetteea accaaageag gagggggeet teacetgetg gteageagte
                                                                       300
actggegece gecateteaa etatggetee eggettgaet atgtgetggg ggacaggaee
                                                                       360
ctggtcatag acacctttca gg
                                                                       382
      <210> 368
      <211> 174
      <212> DNA
      <213> Homo sapien
      <400> 368
ccttctccct ctttgacaag gatggagatg gcactatcac caccaaggag ttggggacag
                                                                        60
tgatgagatc cctgggacag aaccccactg aagcagagct gcaggatatg atcaatgagg
                                                                       120
tggatgcaga tgggaacggg accattgact tcccggagtt cctgaccatg atgg
                                                                       174
      <210> 369
      <211> 216
      <212> DNA
      <213> Homo sapien
      <400> 369
aaatctcatg ggttctatta aaaaaatata tatatagggc cccaatccat tgccatcaaa
                                                                        60
```

```
ttgcccttgg acttttccaa ggtatattat ggggttttat gcaaaattcc aagctaccat
                                                                        120
gtaacttttt ttaaccattt aacaaggagg gggaactgtt tcctaccttc tttacatgtt
                                                                        180
gtgcattgtt gtggtccaga aatgccaaac cttttt
                                                                        216
       <210> 370
      <211> 344
      <212> DNA
      <213> Homo sapien
      <400> 370
ccttggtcag gatgaagttg gctgacacag cttagcttgg ttttgcttat tcaaaagaga
                                                                         60
aaataactac acatggaaat gaaactagct gaagcctttt cttgttttag caactgaaaa
                                                                        120
ttgtacttgg tcacttttgt gcttgaggag gcccattttc tgcctggcag ggggcaggtc
                                                                        180
tgtgccctcc cgctgactcc tgctgtgtcc tgaggtgcat ttcctgttgt acacacaagg
                                                                        240
gccaggetee attetecete cetttecace agtgccacag cetegtetgg aaaaaggace
                                                                        300
aggggtcccg gaggaaccca tttgtgctct gcttggacag cagg
                                                                        344
      <210> 371
      <211> 741
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(741)
      <223> n = A, T, C \text{ or } G
      <400> 371
aaattacata totaattgtg tgatttgtta aatgoocatt tottoatota agtgotaagt
                                                                        60
gctaagtgta gcagtttgtt ccctgctaca ctccaaggca caaaggagtt caaggaatgt
                                                                       120
gcaatggaaa tcagttagat gaatgtgtta ggaaccttcc ctttaataaa gctggatccc
                                                                       180
acactagece ctacacecte teateaceaa atatteetge tteeteteac etgeacttge
                                                                       240
tgttctctcc tctgccacac aaatctacct ctcaagccta ggtcccacct gcttcatgac
                                                                       300
aactttccag actattccag aacctttaac catctctgac ctctcatcag atctatgttg
                                                                       360
tacataacac caattaatga gatcattact gctttatgct ctaattgctt cctgtattca
                                                                       420
aaatcttctc tccaaccaca taatgactcc ctaaacttct cttgtatttt ccaatgcctt
                                                                       480
gtacaagcac agaactggtc aatcaataaa tactcactgg ttatttgagg aaaaaatgtt
                                                                       540
gccaagcacc atctttatca gaaaataaat caattcttct aaacttggag aaatcaccct
                                                                       600
attcctagta tgtgatctta attagaacaa ttcagattga gaangngaca gcatgctggc
                                                                       660
agtectcaga gecetegett geteteggna ectecetgee tgggetecca etttggtgge
                                                                       720
atttgaggag cccttcagcc t
                                                                       741
      <210> 372
      <211> 218
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(218)
      <223> n = A, T, C or G
      <400> 372
ccgccagtgt gctggaattc gcccttggcc gcccgggcag gtaccacaac agcaggnctg
                                                                        60
```

WO 00/37643 PCT/US99/30909

```
agtgagaaat ctaccacctt ctacagtagc cccagatcac cggacacaac actctcacct
                                                                        120
qccagcacga caagctcagg cgtcagtgaa gaatccacca cctcccacag ccgaccaggc
                                                                        180
                                                                        218
tcaacgcaca caacagcatt ccctggcagt accttggn
      <210> 373
      <211> 168
      <212> DNA
      <213> Homo sapien
      <400> 373
actgctaggg aatgctgttg tgtgcattga gcctggtcgg ctgtgggagg tggtggattc
                                                                         60
ttcactgacg cctgagcttg tcgtgctggc aggtgagagt gttgtgtccg gtgatctggg
                                                                        120
                                                                        168
gctactgtag aaggtggtag atttctcact caggcctgct gttgtggt
    . <21.0> 374
      <211> 154
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(154)
      <223> n = A,T,C or G
      <400> 374
tgagaaatct accaccttct acagngagec ccanatcace ggacacaaca ctetcacctg
                                                                         60
ccagcacgac aagetcagge gtcagtgaag aatecaccac etcecacage egaccagget
                                                                        120
caacgcacac aacagcattc cctggcagta cctc
                                                                        154
      <210> 375
      <211> 275
      <212> DNA
      <213> Homo sapien
      <400> 375
actgccaggg gacagtgctg tgtcagttga acctgggctg ctgtgggaag ttgttgattc
                                                                         60
ctgactgggg cctgaggtgg tggtgctggc aggtaacagt gttgtatccg ttgagcctgg
                                                                        120
gctgctgtgg gaagttgtag aatgccgact gaggcctggc gtggtggtgc tgtcagggaa
                                                                        180
tgctgttgtg tgcgttgagc ctggtcggct gtgggaggtg gtggattctt cactgacgcc
                                                                        240
                                                                        275
tgagcttgtc gtgctggcag gtgagagtgt tgtgg
      <210> 376
      <211> 191
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(191)
      <223> n = A, T, C \text{ or } G
      <400> 376
actgccaggg gacagtgctg tgtcagttga acctgagctg ctgtgggaag ttgttgattc
                                                                         60
ctgactggag cctgaggtgg tggtgctggc aggtaacagt gttgtatccg ttgagcctgg
                                                                        120
gctgctgtgg gaagttgtag aatgccgact gaggcctgcc gtggtggtgc tgntagggaa
                                                                        180
```

```
tgctgctagc g
                                                                       191
       <210> 377
       <211> 476
       <212> DNA
       <213> Homo sapien
       <400> 377
 ccgccagtgt gctggaattc gcccttggcc gcccgggcag gtacatttcc ttgtagactc
                                                                       60
 tgttaatttc ctgcagctcc tggttggttc tggagcagat gatctcaatg agagagtcct
                                                                      120
 cgtcggttcc cagccccttc atggaagctt ttagctcaga agcgtcatac tgagcaggtg
                                                                      180
 tetteaatag geccaaaate acceteteca getegecaga taaggetegae tteagteete
                                                                      240
 atgcaagttc ctttttggtc cttctctggt aggcgaaggc aatatcctgt ctctgtgcat
                                                                      300
 tgctgcggtt ggtcaaaatg ttgacaatgg tgacctcatc cacacctttg gtcttgatgg
                                                                      360
 ctgtttcaat gttcaaagca tecegeteag catcaaagtt agtatagget ttgacagace
                                                                      420
 catatgcact tgggggtgta gagtgatcac cctccaagcc gagcttgcac aggatt
                                                                      476
       <210> 378
       <211> 455
       <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(455)
      <223> n = A,T,C or G
      <400> 378
agtgtgctgg aattcgccct tggccgcccg ggcaggtaca catcccatct tcaaatttaa
                                                                      60
aatcatattg tcagttgtcc aaagcagctt gaatttaaag tttgtgctat aaaattgtgc
                                                                     120
aaatatgtta aggattgaga cccaccaatg cactactgta atatttcgct tcctaaattt
                                                                     180
cttccaccta cagataatag acaacaagtc tgagaaacta aggctaacca aacttagata
                                                                     240
300
agaaacaaat ttcaaaataa atcacatctt ctcttaaaac ttggcaaacc cttccctaac
                                                                     360
tgtccaagtn tgagcataca ctgccactgg ctttagatac tccaattaaa tgcactactc
                                                                     420
tttcactggt ctgaatgaag tatggtgaaa caagc
                                                                     455
      <210> 379
      <211> 297
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(297)
      \langle 223 \rangle n = A,T,C or G
      <400> 379
ageteggate cetagnacgg eegecagtgt getggaatte gecettageg geggeeeggg
                                                                      60
caggtacaaa gaatcettag acgccatact gagttttaag tteettaatt ectaatttaa
                                                                     120
ggcttctagt gaagcetect cacagtagge tteactagge ceacagtgee ectagacete
                                                                     180
tgacaatccc accctagaca gactttattg caaaatgcgc ctgaagaggc agatgattcc
                                                                     240
caagagaact caccaaatca agacaaatgt cctagatctc tagtgtggna gaactat
                                                                     297
     <210> 380
```

```
<211> 144
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (144)
      <223> n = A,T,C or G
      <400> 380
actitigation analycetti teccagggie tataaaacat taattigitt tiatattita
                                                                         60
ctattttttt gngttttttt gtttttaaat caataagtaa tctaggacta gcattatgtt
                                                                        120
                                                                        144
tgctagacct ggcatttgct cggc
      <210> 381
      <211> 424
      <212> DNA
      <213> Homo sapien
      <400> 381
actittgaat acaagttict gataccactg cactgictga gaatticcaa aactitaatg
                                                                         60
aactaactga cagcttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt
                                                                        120
catgggacta aatgaactaa tgaggataat attttcataa ttttttattt gaaattttgc
                                                                        180
tgattettta aatgtettgt tteecagatt teaggaaact tttttettt taagetatee
                                                                        240
acagettaca geaatttgat aaaatataet Ettgtgaaca aaaattgaga catttacatt
                                                                        300
                                                                        360
ttctccctat gtggtcgctc cagacttggg aaactattca tgaatattta tattgtatgg
taatatagtt attgcacaag ttcaataaaa atctgctctt tgtataacag aatacatttg
                                                                        420
                                                                        424
aaaa
      <210> 382
      <211> 408
      <212> DNA
      <213> Homo sapien
      <400> 382
actictigaat acaagtitict gataccactg cactgictga gaatticcaa aactitaatg
                                                                         60
aactaactga cagcttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt
                                                                        120
catgggacta aatgaactaa tgaggataat attttcataa ttttttattt gaaattttgc
                                                                        180
tgattcttta aatgtcttgt ttcccagatt tcaggaaact ttttttcttt taagctatcc
                                                                        240
acagettaca geaatttgat aaaatataet tttgtgaaca aaaattgaga catttacatt
                                                                        300
ttctccctat qtgqtcgctc cagacttggg aaactattca tgaatattta tattgtatgg
                                                                        360
taatatagtt attgcacaag ttcaataaaa atctgctctt tgtatgac
                                                                        408
      <210> 383
      <211> 455
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(455)
      \langle 223 \rangle n = A,T,C or G
      <400> 383
actcttgaat acaagtttct gataccactg cactgtctga gaatttccaa aactttaatg
```

```
aactaactgn cnncttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt
                                                                       120
 catgggacta aatgaactaa tgaggataat attttcataa ttttttattt gaaattttgc
                                                                       180
 tganncttta aatgtcttgt ttcccagatt tcaggaaact tttttcttt taagctatcc
                                                                       240
 acagcttata gcaatttgat aaaatatact tttgtgaaca aaaattgaga catttacatt
                                                                       300
 ttctccctat gtggtcgctc cagacttggn aaactattca tgaatattta tattgtatgg
                                                                       360
 taatatagtt attgcacaag ttcaataaaa atctgctctt tgtataacag aatacatttg
                                                                      420
 aaaacattgg ttatattacc aagactttga ctaga
                                                                      455
      <210> 384
      <211> 376
       <212> DNA
      <213> Homo sapien
      <220>
<222> (1)...(376)
      <223> n = A, T, C \text{ or } G
      <400> 384
actettgaat acaaggttet gatateactg caetgtetga gaatttecaa aactttaatg
                                                                       60
aactaactga cagcttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt
                                                                      120
catgggacta aatgaactaa tgaggataat attttcataa ttttttattt gaaattttgc
                                                                      180
tgattettta aatgtettgt tteecagatt teaggaaact ttttttett ttaagetate
                                                                      240
cacagettae ageaatttga taaaatatae ttttgngaae aaaaattgag acatttaeat
                                                                      300
tttctcccta tgtgggcgct ccagacttgg gaaactattc atgaatattt atattgnatg
                                                                      360
ggaatatagc attgcc
                                                                      376
      <210> 385
      <211> 422
      <212> DNA
      <213> Homo sapien
      <400> 385
acctgtgggt ttattaccta tgggtttata tcctcaaata cgacattcta gtcaaagtct
                                                                      60
tggtaatata accaatgttt tcaaatgtat tctgtcatac aaagagcaga tttttattga
                                                                      120
acttgtgcaa taactatatt accatacaat ataaatattc atgaatagtt tcccaagtct
                                                                      180
ggagcgacca catagggaga aaatgtaaat gtctcaattt ttgttcacaa aagtatattt
                                                                     240
tatcaaattg ctgtaagctg tggatagctt aaaagaaaaa aagtttcctg aaatctggga
                                                                     300
aacaagacat ttaaagaatc agcaaaattt caaataaaaa attatgaaaa tattatcctc
                                                                     360
attagttcat ttagtcccat gaaattaatt attttctctg cttgatcttg gtggacagtt
                                                                     420
tc
                                                                     422
      <210> 386
      <211> 313
      <212> DNA
      <213> Homo sapien
      <400> 386
caagtaggtc tacaagacgc.tacttcccct atcatagaag agcttatcac ctttcatgat
                                                                      60
cacgccctca taatcatttt ccttatctgc ttcctagtcc tgtatgccct tttcctaaca
                                                                     120
ctcacaacaa aactaactaa tactaacatc tcagacgctc aggaaataga aaccgtctga
                                                                     180
actatectge eegecateat ectagteete ategecetee catecetaeg catectttae
                                                                     240
ataacagacg aggtcaacga tccctccctt accatcaaat caattggcca ccaatggtac
                                                                     300
tgaacctacg agt
                                                                     313
```

PCT/US99/30909

<210> 387 <211> 236 <212> DNA <213> Homo sapien <400> 387 egeceteata ateatettee tratergett ceragreetg targecettt techaacaet 60 cacaacaaaa ctaactaata ctaacatctc agacgctcag gaaatagaaa ccgtctgaac 120 tatcctgccc gccatcatcc tagtcctcat cgccctccca tccctacgca tcctttacat 180 aacagacgag gtcaacgatc cctcccttac catcaaatca attggccacc aatggt 236 <210> 388 <211> 195 <212> DNA <213> Homo sapien <400> 388 acgccctttt cctaacactc acaacaaaac taactaatac taacatctca gacgctcagg 60 aaatagaaac cgtctgaact atcctgcccg ccatcatcct agtcctcatc gccctcccat 120 180 ttggccacca atggt 195 <210> 389 <211> 183 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(183) $\langle 223 \rangle$ n = A,T,C or G <400> 389 taacactcac aacaaaacta actaatacta nnatctcaga cgctcaggaa atagaaaccn cctgaactat cctgcccgcc atcatcctag tcctcatcgc cctcccatcc ctacncatcc + 120 tttacataac agacgaggtc aacgatccct cccttaccat caaatcaatt ggccaccaat 180 ggt 183 <210> 390 <211> 473 <212> DNA <213> Homo sapien <400> 390 acaaagcagc aactgcaata ctcaaggtta aaacattaga aaagcatttg tgtgacaggt 60 atattacagt attatcaaaa tattacattt tcagacttac ttagcagata atcatccacc 120 agagettaaa tetttaaatt attteeatag tettaaaaaa tatgtaatgt cagaatgeat 180 ataaaaagaa tgtaaaagga aacctaaaat acaaatggaa taatgtaaca aataaatatt 240 tgatttcagt aactgttaat aatcagctca acaccaccat tctctctaaa ctcaatttaa 300ttcttatagg aataatgaac tgtcaaatgc catggcataa ttatttattt ccaaqctatc 360 atcaatgatt agaactaaaa aaaatttggc ataaaaaaat cacaattcaq cataaataaa 420 gctattttta gcttcaacac tagctagcat ctctaagaat tqttqaaata aqt 473 <210> 391

117

<210> 391

<211> 216

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(216)
      <223> n = A, T, C \text{ or } G
      <400> 391
attigtatit taggitteet titacattet tittatatge nnictgaeat tacatattit
                                                                         60
ttaagactat ggaaataatt taaagattta agctctggtg gatgattatc tgctaagtaa
                                                                        120
gtctgaaaat gtaatatttt gataatactg taatatacct gtcacacaaa tgcttttcta
                                                                        180
atgttttaac cttgagtatt gcagttgctg ctttgt
                                                                        216
      <210> 392
      <211> 98
      <212> DNA
      <213> Homo sapien
      <400> 392
acttatttca acaattctta gagatgctag ctagtgttga agctaaaaat agctttattt
                                                                         60
atgctgaatt gtgatttttt tatgccaaat ttttttaa
                                                                         98
      <210> 393
      <211> 397
      <212> DNA
      <213> Homo sapien
      <400> 393
tgccgatata ctctagatga agttttacat tgttgagcta ttgctgttct cttgggaact
                                                                         60
gaactcactt teeteetgag getttggatt tgacattgea tttgacettt tatgtagtaa
                                                                        120
ttgacatgtg ccagggcaat gatgaatgag aatctacccc cagatccaag catcctgagc
                                                                        180
aactcttgat tatccatatt gagtcaaatg gtaggcattt cctatcacct gtttccattc
                                                                        240
aacaagagca ctacattcat ttagctaaac ggattccaaa gagtagaatt gcattgaccg
                                                                        300
cgactaattt caaaatgctt tttattatta ttatttttta gacagtctca ctttgtcgcc
                                                                        360
caggccggag tgcagtggtg cgatctcaga tcagtgt
                                                                        397
      <210> 394
      <211> 373
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(373)
      <223> n = A, T, C or G
      <400> 394
ttacattgtt gagctattgc tgttctcttg ggaactgaac..tcactttcct cctgaggctt
                                                                         60
tggatttgac attgcatttg accttttatg tagtaattga catgtgccag ggcaatgatg
                                                                        120
aatgagaatc tacccccaga tccaagcatc ctgagcaact cttgattatc catattgagt
                                                                        180
caaatggtag gcatttccta tcacctgttt ccattcaaca agagcactac attcatttag
                                                                        240
ctaaacggat tccaaagagt agaattgcat tgaccacgac tantttcaaa atgcttttta
                                                                        300
ttattattat tttttagaca gtctcacttt gtcgcccagg ccggagtgca gtggtgcgat
                                                                        360
ctcagatcag tgt
                                                                        373
```

```
<210> 395
      <211> 411
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (411)
      \langle 223 \rangle n = A,T,C or G
      <400> 395
actgatcatt ctatttcccc ctctattgat ccccacctcc aaatatctca tcaacaaccg
                                                                         60
                                                                        1.20
actaatcacc acccaacaat gactaatcaa actaacctca aaacaaatga taaccataca
caacactaaa ggacgaacct gatctcttat actagtatcc ttaatcattt ttattgccac
                                                                        180
aactaacctc ctcggactcc tgcctcactc atttacacca accacccaat tatctataaa
                                                                        240
cctagccatg gccatcccct tatgagcggg cgcagtgatt ataggctttc gctctaagat
                                                                        300
taaaaatgcc ctagcccact tcttacngca aggcacacct acacccctta tccccatact
                                                                        360
                                                                        411
agitattato gaaaccatca gootactcat toaaccaata gooctggoog t
      <210> 396
      <211> 411
      <212> DNA
      <213> Homo sapien
      <400> 396
                                                                        60
actgatcatt ctatttcccc ctctattgat ccccacctcc aaatatctca tcaacaaccg
actaattacc acccaacaat gactaatcaa actaacctca aaacaaatga tagccataca
                                                                        120
caacactaaa ggacgaacct gatctcttat actagtatcc ttaatcattt ttattgccac
                                                                        180
                                                                      240
aactaacctc ctcggactcc tgcctcactc atttacacca accacccaac tatctataaa
cctagccatg gccatcccct tatgagcggg cgcagtgatt ataggctttc gctctaagat
                                                                        300
                                                                        360
taaaaatqcc ctaqcccact tcttaccaca aggcacacct acacccctta tccccatact
                                                                        411
agttattatc gaaaccatca gcctactcat tcaaccaata gccctggccg t
      <210> 397
      <211> 351
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(351)
      <223> n = A, T, C or G
      <400> 397
ngccgangta caaaaaaaag cacattccta gaaaaaggta ttggcaaata gtaaaaatgg
                                                                         60
gaggtcaaaa ncaaaaaaaa aaaaaacaaa acnaaaaaaa gaaaaaacca acaattcttc
                                                                        120
aattcagtgt gcaaacatta tataaaaata gaaatactaa ctctacaggc agtatttcct
                                                                        180
gataaattat ttaaatagca tatctacnca atctgagata tctattccaa tggcaatgag
                                                                        240
                                                                        300
aaaataattt ataaaaataa aqcaatqqta taccanatga tagaaaaaaa cataactttc
agaaattgta tttaacattt caatgctatt tccttattgn gaatncttct c
                                                                        351
      <210> 398
      <211> 363
      <212> DNA
```

<213> Homo sapien

```
<400> 398
acaaaaaaaa gcacattcct agaaaaaggt attggcaaat agtaaaaatg ggaggtcaaa
                                                                      60
agcaaaaaaa aaaaaaacaa aacaaaaaaa agaaaaaacc aacaattctt caattcagtg
                                                                     120
tgcaaacatt atataaaaat agaaatacta actctacagg cagtatttcc tgataaatta
                                                                     180
tttaaatagc atatctacac aatctgagat atctattcca atggcaatga gaaaataatt
                                                                     240
tataaaaata aagcaatggt ataccagatg atagaaaaaa acataacttt cagaaattgt
                                                                     300
atttaacatt tcaatgctat ttccttattg ggaatacttc tctgcagagt ttttatgcta
                                                                     360
tgt
                                                                     363
      <210> 399
      <211> 360
      <212> DNA
      <213> Homo sapien
      <400> 399
actgtttcct cgtggttcag gggtgtgcat gaaggctctt aggagagcaa acacctgttc
                                                                     60
ctattctgta tgtccctccc tcatttcaaa tgagagtaac caattgagta aaataaccaa
                                                                    120
ataaccattg ccccaccatg aacatggggc ttgggaagac agtcctacaa tcttcatcat
                                                                    180
atatttaggt ttttaggcca gccagctctt tttttccaaa gctttctttt gaatacccgc
                                                                    240
ccgggcggcc cctaagggcg aattctgcag atatccatca cactggcggc cgctcgagca
                                                                    300
tgcatctaga gggcccaatt cgccctatag tgagtcgtat tacaattcac tggccgtcgt
                                                                    360
      <210> 400
      <211> 87
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(87)
     <223> n = A,T,C or G
      <400> 400
ctgcacatat cnattacact ggcggccgct cgagcatgca tgnagagggc ccaattctcc
                                                                     60
ctatattgag tggaattaca atnonct
                                                                     87
      <210> 401
      <211> 328
      <212> DNA
      <213> Homo sapiera
      <220>
      <221> misc feature
      <222> (1)...(328)
      <223> n = A,T,C or G
      <400> 401
acccagggac acaaacactc tgcctaggaa aaccagagac ctttgttcac ttgtttatct
                                                                     60
gctgaccttc cttccactat tgtcctatga ccctgccaaa tccccctctg cgagaaacac
                                                                    120
180
ccacaaaaaa aaaaaaaaa aaagtntata aaataaaata ttgaagtcct ttcccattaa
                                                                    240
aaaaaaaaaa aagaaaaagc acggactctt tcatccagtt ctgatgtgat tatctctgga
                                                                    300
aggcattttc tcctcctctt ccctcccc
                                                                    328
```

WO 00/37643 PCT/US99/30909

```
<210> 402
      <211> 268
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(268)
      <223> n = A, T, C or G
      <400> 402
nacataatga caacatette actagactga gtgttcaagg atttgagatg attcgctatt
                                                                        60
catcacaccc cgaagattga gatccactgt atttacacaa agcaaagcca tgtcagcaag
                                                                       120
ggactgtcaa cctgattctg agaacataaa cattcaaaat ttattttcca gtgttccttt
                                                                       180
ttggaaacca acaacacatc tttaatacct acacacacac acatctntac ctttaaaaaa
                                                                       240
aaaaaaaag tgnaacttca cagatagt
                                                                       268
      <210> 403
      <211> 538
      <212> DNA
      <213> Homo sapien
      <400> 403
acagtgatag ctccccctgg gcaatacaat acaagaacag tgggttttgt caaattggaa
                                                                        60
caaggaaaca gaaccacaga aataaataca ttggttaaca tcagattagt tcaggttact
                                                                     . 120
tttttgtaaa agttaaagta gaggggactt ctgtattatg ctaactcaag tagactggaa
                                                                       180 -
totootgtgt tottttttt tttaaattgg ttttaatttt ttttaattgg atctatotto
                                                                       240
ttccttaaca tttcagttgg agtatgtagc atttagcacc actggctcaa tgcgctcacc
                                                                       300
taggtgagag tgtgaccaaa tcttaaagca ttagtgctat tatcagttac caccatttgg
                                                                       360
ggcttttatc cttcatgggt tatgatgttc tcctgatgac acatttctct gagttttgta
                                                                     . 420
attccagcca aagagagacc attcactatt tgatggctgg ctgcatgcag acatttaaag
                                                                       480
cttttagaga atacactaca ccagggagta tgactactag tatgactatt aggagggt
                                                                       538
      <210> 404
      <211> 310
      <212> DNA
      <213> Homo sapien
      <400> 404
ttttttttata gatacaattg gcttttattt gtgattcatg agtcagggca gtttccattc
                                                                        60
tgcaaaatat agtgatagct cctactgggc aatacaacag tagaacagtg ggttttgtaa
                                                                       120
aatgggaatc caggaacaga agaatataaa taaattgatt taaataaact gattggttaa
                                                                       180
tttcagaata cttcatatta ctttttcta agagttaaag cagaaaggac tttcttactg
                                                                       240
tgctgactca gacagcctgg actctcatgt ttttaggaaa attttgtctg ttctgggatc
                                                                       300
tacctgcttc
                                                                       310
      <210> 405
      <211> 559
      <212> DNA
      <213> Homo sapien
      <400> 405
acaaatcaca attattaact cactggtagg gcagtgatga tcaaaccaat tgcattcatc
                                                                       60
catgctgtaa tgttctctct tggcactaaa ggctgactgc agccggcaaa aaagaatgta
                                                                       120
```

```
agtatgaatt tataaaaaca ttttagatgg ctgacaacgg atcttatttt taaagaatat
                                                                        180
  gtctaattca gaggatcgac aactaatcca tttcaataaa acaatgggga attttttatt
                                                                        240
  gaataaaaat gtaatatgca taaaaactca agaaggcttt ttaaaaaatac ttcctcccca
                                                                        300
  atcattatcc catacttcat gctaattttt aaaagaatct tgaaatcttg aaaacaagat
                                                                        360
  gaagagaatc ttgttttaag tgacaagtta acattattcc tatattaaat gtcaaactgc
                                                                        420
  tattaatgag tagaagtagg aacaaacccg gatcttagga tcctgtccaq qqctcattcc
                                                                        480
  ataactccta tatcacaaag acaagatctg gaaccagaaa acagtcatca tccaatgtgc
                                                                        540
  atcagccttg cggcaacag
                                                                        559
        <210> 406
        <211> 427
        <212> DNA
        <213> Homo sapien
acaacagaat atctcgggaa tggactcaga agtatgccat gtgatgctac cttaaagtca
                                                                         60
 gaataacctg cattatagct ggaataaact ttaaattact gttcctttt tgatttctt
                                                                        120
 atcoggotgo toccotatoa gacotoatot tttttaattt tattttttgt ttacctccct
                                                                        18û
 ccattcattc acatgctcat ctgagaagac ttaagttctt ccagctttgg acaataactg
                                                                        240
 cttttagaaa ctgtaaagta gttacaagag aacagttgcc caagactcag aatttttaaa
                                                                        300
 aaaaaaaatg gagcatgtgt attatgtggc caatgtcttc actctaactt ggttatgaga
                                                                        360
 ctaaaaccat tecteaetge tetaacatge tgaagaaate atetgagggg gagggagatg
                                                                        420
 gatgete
                                                                        427
       <210> 407
        <211> 419
        <212> DNA
        <213> Homo sapien
        <400> 407
 acaatttgta gttgtttcca ggtttggcta ataatcattc cttaacctag aattcagatg
                                                                         60
 atcctggaat taaggcaggt cagaggactg taatgataga attaaattag tgtcactaaa
                                                                        120
 aactgtccca aagtgctgct tcctaatagg aattcattaa cctaaaacaa gatgttacta
                                                                        180
 ttatatcgat agactatgaa tgctatttct agaaaaagtc tagtgccaaa tttgtcttat
                                                                        240
 taaataaaaa caatgtagga gcagcttttc ttctagtttg atgtcattta agaattacta
                                                                        300
 acacagtggc agtgttaaat gaagatgctg tctacaaggt agataatata ctgtttgata
                                                                      360
 ctcaaaacat ttttcatttt gtttaaagta gaagttacat aattctatat tttaagtct
                                                                        419
        <210> 408
       <211> 523
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(523)
       <223> n = A, T, C \text{ or } G
       <400> 408
 acattigatg ttaigigaat giigagiitt titcitctaa tittcactic agcagigitt
                                                                         60
 agggctttca gatgccttat tccagtgtga acagaaaaag ttcatatttt atgtggttaa
                                                                        120
 tgctttgatg tgtcacataa agagtagttt gtagaaaatg ttggcacaat tttaacttct
                                                                        180
 tagtggcttg tgacattata tattatatat atatgtatat atatctttat aacattcctg
                                                                        240
 tgtttagtag tgtaaatgtt ctgggcaagt tttaatattt tgaatgcctt tggatattcc
                                                                        300
 agcaataaag gcatcatgtt ctgcaatagg atttcttact catttaccta ttttaacact
                                                                        360
```

WO 00/37643 PCT/US99/30909

```
420
aaaatagacc acaactgagc acaaattcct tttataaatg ttatagaagc agggaagaat
aataaacaca tttgtgaatt gtggttcagt ttatttatct ttagggaagg ctgatcattt
                                                                        480
atcttatagc acataacccc agcctcttat tcattatggn taa
                                                                       .523
      <210> 409
      <211> 191
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(191)
      <223> n = A, T, C or G
      <400> 409
accordingt gatgageact gattggttca ctggccacat tttagttctt cataataata
                                                                         60
ggccacaaaa gggctctgtg gtttgcctcc atgtgcactg gcccctcccc acccctaggg
                                                                        120
                                                                        180
ggcactcagt agctgctgag aaggcctgtc cacgangctg ttggaacccc ttcaataaat
                                                                        191
acttagaagn a
      <210> 410
      <211> 403
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(403)
      \langle 223 \rangle n = A,T,C or G
      <400> 410
                                                                         60
acactggcca gtgtgttttt ggcgattaaa cataatcctg tgaatcagat taattcactt
gctgagtgtt catttgcggc atccctctgt tgggtcttgg gggccctcca cgacctcgtg
                                                                        120
                                                                        180
gggctccccg tggtccactc tgcccagagc ctcgcttgaa attctgctga tatccatccc
gttgatagcc agagtaatcc cggggagcac tgaactgaga ctgtgtataa ccactgtttg
                                                                        240
                                                                        300
gagtgttaga gaatgaaggg cggtaaccat catateetee tetgaateea ttggcaggge
cccggtatcc attcatcaag cctctagcac cacgggagcc tccacgagac acaccacgac
                                                                        360
tattgtaata gggctgattg ctacgtggaa atccagtgnt ctg
                                                                        403
      <210> 411
      <211> 384
      <212> DNA
      <213> Homo sapien
      <400> 411
acgtgaaatc ataacaacat gttctcttgt gtttggcttc tcttgctcag catgatattt
                                                                         60
ttacggttca cccatattgc atgtatcagg aatataatcc tttttattat tgagtagtgt
                                                                        120
tctattgtat gtatatacca cagtttattt ctcccttcat cctttgctag attttggggt
                                                                        180
                                                                        240
tttttcacat tgcgctattc aagtataaac ctgctctcaa cattcatgtg caagtctttg
agtggacata tatttgccgt ttctcttgag tgaatgcacc ttgttgggtc acgtggctta
                                                                        300
atttaaaaaa attttaatca ctgtggtgca tatgtagtga ttattagtga ttatctcata
                                                                        360
                                                                        384
attttatttt cttgatgact aatg
      <210> 412
      <211> 315
```

```
<212> DNA
           <213> Homo sapien
           <220>
           <221> misc_feature
           <222> (1)...(315)
           <223> n = A,T,C or G
           <400> 412
     acaatatttc tcctttgaga agataggata tatgattttc ccaaaaatca caactttgaa
                                                                           60
     ggaagactta nttgctgact tcaattatat cctggaactg gcaacttgtg cccttccttt
                                                                          120
     gcttcaaaaa aagtgtaaga aagagtgata agatcaactt taatcattct tggatcttca
                                                                          180
     gcaaattcag gatcaatgta gaaaaacact ggcatatcta cttcctcttg gggattaagc
                                                                          240
     ctttgttctt caaaacagaa gcactgtatt ttartgaaat actgtccacc ttcaaatqqa
                                                                          300
3-1×5×
           <210> 413
           <211> 554
           <212> DNA
           <213> Homo sapien
           <220>
           <221> misc feature
           <222> (1)...(554)
           \langle 223 \rangle n = A,T,C or G
           <400> 413
     acaggittica ciattacaaa tataigaigi taaactaada aacicaigac ciicaaagai
                                                                           60
     gtottogtoc cacgoacaca cattigtaat tigigtocat tigotatito cottottota
                                                                          120
     taatcttcaa attatatagt tatgcattga gttccctatg catctcaccc atctccttta
                                                                          180
     tetcageett etcataettt gecattetet tetttetgga aataaccage acaacaatte
                                                                          240
     cagcaacaac tgctatcacc acaaccacaa taacagcaat aacaccagct tttagaccct
                                                                          300
     gcattgagaa ttcaggtgct ttttcatcaa cataataaat taaagtttga ccaggatcca
                                                                          360
     gatccagttg ttccccattt actgtcaggt gccattttct tagaatgaaa caaggattca
                                                                          420
     cctttaacat ctttttcaaa ataataagcc acatcagcta tgtccacatc attctgagnt
                                                                          480
     ttttgagaag aattttgaac cagatcaata gtgataacat tattctcata caaaatactc
                                                                          540
     gngataaatt ntgg
                                                                          554
           <210> 414
           <211> 267
           <212> DNA
           <213> Homo sapien
           <400> 414
     accagaaagg cacacgattt tacaatattt gttggaatta ccttactttt taacctcctc
                                                                           60
     atagcagttt tggtttgagt atattgatga aagccaaagt ctggtatcta aaacttgggc
                                                                          120
     caatgtttcc caactggtat atgtcaggct ttcccaatag cttaactgtg accctatacg
                                                                          180
     gatggctttt tagatagttc tatactgctg tattgtgtta gcacttttct ttgtcattaa
                                                                          240
     caacacactt taaatgacat ttggtga
                                                                          267
           <210> 415
           <211> 454
           <212> DNA
           <213> Homo sapien
```

```
<400> 415
accqgaacct gcagaaacag tgtgagaaat taagtcctgg ttcactgcgc agtagcaaag
                                                                      60
atggtcaagg ccatggaaaa agcagaaatt taccaagaaa gctgataccc atgtatagtt
                                                                     120
cccactcatc tcaaatacat ctgctatctt tttaagctaa gtcctagaca tatcggggat
                                                                     180
aacatqqqqq ttqattagtg accacagtta tcagaagcag agaaatgtaa ttccatattt
                                                                     240
                                                                     300
tatttgaaac ttattccata ttttaattgg atattgagtg attgggttat caaacaccca
                                                                     360
caaactttaa ttttgttaaa tttatatggc tttgaaatag aagtataagt tgctaccatt
                                                                     420
ttttgataac attgaaagat agtattttac catctttaat catcttggaa aatacaagtc
ctgtgaacaa ccactctttc acctagcagt atga
                                                                     454
      <210> 416
      <211> 370
     <212> DNA
      <213> Homo sapien
      <400> 416
ccgacacggt gccagcgccc tgctgcgtgc ccgccagcta caatcccatg gtgctcattc
                                                                      60
aaaagaccga taccggggtg tcgctccaga cctatgatga cttgttagcc aaagactgcc
                                                                     120
actgcatatg agcagtcctg gtccttccac tgtgcacctg cgcggaggac gcgacctcag ...
                                                                     180
ttgtcctgcc ctgtggaatg ggctcaaggt tcctgagaca cccgattcct gcccaaacag
                                                                     240
                                                                     300
ctgtatttat ataagtctgt tatttattat taatttattg gggtgacctt cttggggact
cgggggctgg tctgatggaa ctgtgtattt atttaaaact ctggtgataa aaataaagct
                                                                     360
                                                                     3.70
gtctgaactg
      <210> 417
      <211> 463
      <212> DNA
      <213> Homo sapien
      <400> 417
acactttata tattccaaat tgatcagata tatggtttgc aaattcatct caatctgtag
                                                                    . 60
cttatctttt cctcttctta aatcacaagt ttttaaattt tgaagaagtc caatatatca
                                                                     120
gattttgtct tttatggatg tgctttcggg gcaaagtcca agaacttgtc acctagccca
                                                                     180
agateetgaa gatttttete etgtggettt ttteaaagtt atetagtttt atgtateaca
                                                                     240
                                                                     300
tttaagtccg ttatacattt tgagttaaat tttatataag argtgaggtt taagtagagg
ttetttttte teetegeeat gggtgtetaa ttgetetage ataatttgte agaaaggeta
                                                                     360
ttcttcctcc attgaattgc tttttcactt tttcaaaatc agctgagcat atttatatgg
                                                                     420
gtttatttct gggttctctc atctgttcca ttgacgtatg tgt
                                                                     463
      <210> 418
      <211> 334
      <212> DNA
      <213> Homo sapien
      <400> 418
ttagcatttg cttttatttt tttactttga tgccttttca aattggcatg tctttaaagt
                                                                     60.
120
ttttaaatca cattaatttt accaagtgaa accaagccat actgtttttg agccaattaa
                                                                     180
gaaaattgcc atttttaaag tgtagcattt cagggtaaag acccatgaaa tggcttgatg
                                                                     240
tattctagac tactgaaaga aaaccacttc aaagattttg ttgaaagttt tagtgttgtc
                                                                     300
tgaaatgcaa gagggaaggt gattggtagt gagt
                                                                     334
      <210> 419
      <211> 297
```

<212> DNA

```
<213> Homo sapien
      <400> 419
acticitiga ccaaggaata ccacagacac cctaccgata gaacagtggc tcagatctta
                                                                        60
cttgctcctg cttacgaagt attcccaatc actggtcatc tgaccctact tgaacactcc
                                                                       120
tgaacagtca tgttttttaa aatcttcctt tatatcaagt cagagagtat acttctataa
                                                                       180
atttcactca tggatgttag gaaatctagt catcttccct gtgattgccc tgttaagtat
                                                                       240
ttaaccatag ctatcatgtg tttcccaaat cttctctaga ttaaatatct tcaqtta
                                                                       297
      <210> 4.20
      <211> 418
      <212> DNA
      <213> Homo sapien
      <400> 420
acgagaggaa ccgcaggttc agacatttgg tgtatgtcct atcaatagga gctgtatttg
                                                                        60 -
ccatcatagg aggetreatt cactgattte ccctattete aggetacace etagaccaaa
                                                                       120
cotacgocaa aatocattto gotatoatat toatoggogt aaatotaact ttottoccac
                                                                       180
aacactttct cggcctatcc ggaatgcccc gacgttactc ggactacccc gatacataca
                                                                       240
ccacatgaaa tatcctatca tctgtaggct cattcatttc tctaacagca gtaatattaa
                                                                       300
taattttcat gatttgagaa geettegett egaagegaaa agteetaata gtagaagaac
                                                                       360
cotecataaa cotggagtga ctatatggat goodcocaco ctaccacaca ttoqaaqa
                                                                       418
      <210> 421
      <211> 304
      <212> DNA
      <213> Homo sapien
      <400> 421
acgcctggac ccctgtgact tgcagcctat ctttgatgac atgctccact ttctaaatcc
                                                                        60
tgaggagetg egggtgattg aagagattee eeaggetgag gacaaactag accggetatt
                                                                       120
cgaaattatt ggagtcaaga gccaggaagc cagccagacc ctcctggact ctgtttataq
                                                                       180
ccatcttcct gacctgctgt agaacatagg gatactgcat tctggaaatt actcaattta
                                                                       240
gtggcagggt ggttttttaa ttttcttctg tttctgattt ttgttgtttg gggtgtgtgt
                                                                       300
gtgt
                                                                       304
      <210> 422
      <211> 578
      <212> DNA
      <213> Homo sapien
      <400> 422
actgtgcagg cagattcaca gggtggtggt aaagcatcca caatggctct ggcagcatca
                                                                        60
ggatcacact tgaaggggct ctcagacaaa gttgtattca tgcaactgat tccttttcca
                                                                       120
ttcgttttct tagtcactaa tgctttccaa tggtcatgag tgcttttaat aatatcaatq
                                                                       180
gcaaagtcct tatctttaaa ttctgcatta aacgcaaact cattttctgg ttttccatca
                                                                       240
ggaaccttat accttctaaa ccagtccaca gtagcttcta agtagccagg tttcagccgt
                                                                       300
ttgacatcat tgatatcatt ataattggct gcatcaggat catccacatt aatggcaatg
                                                                       360
actiticcagi eggitticece tiegicaate atagecaata igeetagaae titeaattat
                                                                       420
ttatttcacc tcttgcacat accttgcttc caatttcaca cacatcaatt gggtcattgt
                                                                       480
caccacaaca gccagtatgt ttatcattgt gccctgggtc ttcccaagtc tgagggatgg
                                                                       540
caccatagtt ccagatatat cctttatacg ggaacaaa
                                                                       578
      <210> 423
```

<211> 327

PCT/US99/30909

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(327)
      <223> n = A,T,C or G
      <400> 423
acagtatatt tttagaaact catttttcta ctaaaacaaa cacagtttac tttagagaga
                                                                       60
ctgCaataga atcaaaattt gaaactgaaa tctttgttta aaagggttaa gttgaggcaa
                                                                       120
gaggaaagcc ctttctctct cttataaaaa ggcacaacct cattggggag ctaagctagg
                                                                       180
tcattgtcat ggtgaagaag agaagcatcg tttttatatt taggaaattt taaaagatga
                                                                       240
tgyaaagcac atttagcttg gtctgaggca ggttctgttg gggcagtgtt aatggaaagg
                                                                       300
gctcactgrit gntactacta gaaaaat
                                                                       327
      <210> 424
      <211> 384
      <212> DNA
      <213> Homo sapien
      <400> 424
acgaaaaata aatctcctta aaaactaaat aaaatgcact gtattcttac agttaatgtt
                                                                       60
tataactata gtaaaaaatt aatatatatc ctattacata aatgttattt cttaggtgtt
                                                                      120
ccattaagaa gagcaataga ataatgctaa aaaataatgc ctataaatct tcagagtata
                                                                      180
aagacatcca ttcagaaaca aaaattagca ctaaattttt tataaaatag accagatgac
                                                                      240
aaaatttatt ttatttttaa acagtggttt tgacacaaat tatgttattg aaaagcatta
                                                                      300
ttaatgttta atttattaa aattttggaa tttgccattt ctcagagaat gatcaggcct
                                                                      360
taggaaatta atacagtagt agta
                                                                      384
      <210> 425
      <211> 255
      <212> DNA
      <213> Homo sapien
      <400> 425
actatcaggc tttgtgctga tttcctgaac aaactgcatt atattatgaa aacaaaagga
                                                                       60
aaagaagaaa taataaaaac tatactccca tatttcactt acagtgtttg agttcctgga
                                                                      120
aggacctata taatggaggc agcattcaaa caagaaatta tgccaatcaa ctgtcaaatt
                                                                      180
ttcactataa ttttcctaaa aaggcgtttt tcccccaata tctattaatc tcaaagaaac
                                                                      240
ataagttgtg aatgt
                                                                      255
      <210> 426
      <211> 196
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
     <222> (1)...(196)
     <223> n = A,T,C or G
      <400> 426
acatgaantn nccaggccca cacagccaga cagcaacaga accaagacct agggctcttc
                                                                       60
actectgtta cateacacea tggcaatgat tttacattet ceaactgatt caaateatat
                                                                      120
```

WO 00/37643

```
ggcagctagg gatttggggg ctccatgttt tatttcaatt gcaagttcaa gatttctttt
                                                                                                                                                                                                180
                                                                                                                                                                                                 196
                    tatctttgtg ggctga
                                   <210> 427
                                   <211> 163
                                   <212> DNA
                                   <213> Homo sapien
                                   <400> 427
                    acagaagatc catggaggca agtgctgtca ggaaggacac tgcctccctc caccctccca
                                                                                                                                                                                               60
                    aatgtcacca ccaagttcct tcaggtgaga cctcacacaa tgtcaagtgc tttctaggaa
                                                                                                                                                                                                120
                    atactaagat caggttgaga gattctgctt ggtctagtca atc
                                                                                                                                                                                                163
                                   <210> 428
no comunidado en sen se mensiones como mensiones de Textura Grit e Zonnica inno compresa, com comunidade estambando
                                                                                                             mania e nice cario antigo de principal de pr
                                   <212> DNA
                                   <213> Homo sapien
                                   <220>
                                   <221> misc_feature
                                   <222> (1)...(315)
                                   \langle 223 \rangle n = A,T,C or G
                                   <400> 428
                    nactgagtan agatgctggg gaatgtgcaa tatgccttga agaattgcag cagggagata
                                                                                                                                                                                                  60
                    ctatagcacg actgccttgt ctatgcatat atcataaagg ctgcatagat gaatggtttg
                                                                                                                                                                                                120
                    aagtaaatag atcttgccct gagcaccctt cagattaagc gtcagcttcc tgttttatag
                                                                                                                                                                                                180
                    gttttcttgt cttgacaaga tgcttgaaaa accaagagga tatgaaaatc tgtctctgga
                                                                                                                                                                                                240
                    gaaacaaaga cgcaggcata ctcagccaga aatctgagtt ttgtgagact tggtaataca
                                                                                                                                                                                                300
                    gagatggaca atcgt
                                                                                                                                                                                                315
                                   <210> 429
                                   <211> 131
                                   <212> DNA
                                   <213> Homo sapien
                                   <220>
                                   <221> misc_feature
                                   <222> (1)...(131)
                                   \langle 223 \rangle n = A,T,C or G
                                   <400> 429
                     acagttaggn actagaacat ttgttaagcc tcccaaagta gngtgcatgg aagattctag
                                                                                                                                                                                                  60
                     agtgtccagc tcttgcacta caaatgtaat aataacagaa taaatacact taccctgatg
                                                                                                                                                                                                120
                     atattgaggg t
                                                                                                                                                                                                131
                                   <210> 430
                                   <211> 503
                                   <212> DNA
                                   <213> Homo sapien
                                   <400> 430
                     actgattttt aataaaagaa ataaggttca aagtttagca caacaacaca gcaataagaa
                                                                                                                                                                                                 60
                     gctgacaact tggataaaaa tacaagaaag taacacagag cccaggctac ccattattta
                                                                                                                                                                                                120
                     ctgtgtgcat acaggaatgc tatacttcag atgtataaat tagagactga ttttaagtta
                                                                                                                                                                                                180
```

WO 00/37643 PCT/US99/30909 129

```
ttaatttaac tactttttgt ccactgtgct aaactaaatt ttatactaat gtgctactgc
                                                                     240
gtaaacactt caaagcaatc ttcattaaaa tgctgcaaag aaaaacaaga atacacatca
                                                                     300
tccaaaacta aggatgtcat tgcagttcac agtttgtata ataaataccc tccctttcaa
                                                                     360
tcactactaa gatcactaca tcctatctac tcatcagcac aaccttgaag caacttatac
                                                                     420
ttacaaatat tagcaatgca gccaaacatt tgttttttgc aaagcaacta gtaaaaatca
                                                                     480
agaattttaa ttaagacggt gca
                                                                     503
      <210> 431
      <211> 207
      <212> DNA
      <213> Homo sapien
      <400> 431
acaagtgtgg cctcatcaag ccctgcccag ccaactactt tgcgtttaaa atctgcagtg
                                                                      60
gggccgccaa cgtcgtgggc cctactatgt gctttgaaga ccgcatgatc atgagtcctg
                                                                     120
tgaaaaacaa tgtgggcaga ggcctaaaca tcgccctggt gaatggaacc acqqqaqctq
                                                                     180
tgctgggaca gaaggcattt gacatgt
                                                                     207
      <210> 432
      <211> 485
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(485)
      <223> n = A,T,C \text{ or } G
      <400> 432
aaaaaaagta atggaaaaat ggttgcaggt ttaatcncaa aangaactta attttnqtnq
                                                                      60
attitigttit atcigctaaa acactaatat ctataaatat gaactgacag catcgttcta
                                                                     120
aatttacttc tgaagagctg tcgagacttc aataaaatat aagcaagtta ctggatcata
                                                                     180
tttatggact gctgaattaa ctacccgaaa agtatcagtt actttcaaag aacacaaaac
                                                                     240
aaagtgaacg tggaaaaaag ccttctttgc aaaagtcctt ttattagtcc tatcctctaa
                                                                     300
aattccaagc cacagagcct tgatattcct ggattctgtt ttaagtaacc ttagttttaa
                                                                     360
420
cttttttcca aaggnagnca ttttctttaa atncatccta tccacttttg cccacttccc
                                                                     480
catqt
                                                                     485
     <210> 433
      <211> 280
     <212> DNA
     <213> Homo sapien
      <400> 433
actgtcacta caatattaca ttctgcaaat gttattctgt tgtatcagat acaaaatttt
                                                                      60
agtgaggtat ctctaaggca catagtagaa aacaaaattg gttaattact caagttcctt
                                                                     120
tcactgtgat ttggaaatga tttaatcttt atagaatgag aacctttttt ggactagctt
                                                                     180
ttttattaaa atggctcaat ttgtgttgat aaggattgca ttaatattta atagtgcttg
                                                                     240
cttttcctct gggcacacca ttttgatcat taaccagagt
                                                                     280
     <210> 434
     <211> 234
     <212> DNA
     <213> Homo sapien
```

```
<400> 434
ctttgctgcg catcaggtgc tttaagcttc ggaacaactg tgcaggattc tattttagta
                                                                        60
ttctggaagc atcattgagg aagtagtcca gtgaagttag ctctaaaaaa actctttact
                                                                        120
ctaacaatta aaagaaatat gccaaaggat ccataaggga tgaataaatt attaaactat
                                                                        180
taagaagttg ctataaatat gcagtgttaa ttcaataatt cataacggac tggt
                                                                        234
       <210> 435
       <211> 330
      <212> DNA
      <213> Homo sapien
      <400> 435
acctecegtg teaccagtte ceacagaage actgeaaaae tecacatgte tgetgagegt
                                                                        60
ctgtttgtgt cttcaggctt cttctgcaga gcttcggggg ctacccaggc aggtgcatac
                                                                       120
atgcgaccag gacattggaa agagaacttg acatcagcca tgctaattcg ggcagtcatg
                                                                       180
tcctcatcaa tcattacact acggctattg agtgcatgtc gtgggatgag gggctctagt
                                                                       240
gtgtgtagga aagccatgcc ccttgccatg tccaaagcaa acttcacagc ctggctctgg
                                                                       300
tccacgacga aattggtgcc ttcatgtagt
                                                                       330
      <210> 436
      <211> 311
      <212> DNA
      <213> Homo sapien
      <400> 436
acaactttac aatggaattg tatttcaatg attattttga tatcagatta aaccttccaa
                                                                        60 ·
aaagttacac ataattcagg tctattttt ctaccagtaa gagttctgct aaattacaaa
                                                                       120
accccataat cacagtgttc agtttttaaa aaattaaaca cacagtaatc ctgtcaatgt
                                                                       180
raatcaaaat caaaacttcg gaatgeegtg geatttatgt gaccaatetg agttttagat
                                                                       240
acaaatacca gctgtttatc ccatgaacca tttttcctag gctgaggctg tgaaaaatcg
                                                                       300
aaagtcggcg t
                                                                       311
     <210> 437
      <211> 355
      <212> DNA
      <213> Homo sapien
      <400> 437
actagtggat gggggtcagg gtgtcactcc aaggccctct acagacccag agaagaggaa
                                                                       60
agtcaaaaaa gccagatatg agactgctga agtggtgtta agaaatatag gcaaggtaaa
                                                                       120
gggaacaaga tctgggctcc ctcctacttg tgtccctcac tggacctcag acaccctacc
                                                                       180
tctaagactg gttcttagaa ggctgaacag taaggagcat tccaatagct tctgaaactc
                                                                       240
ccaaggctgt ttcaagtagt cgaaagccat ccctggactg ttcaggtgcc ttttctattt
                                                                       300
cccacctgag ctctctgccc tttctttgag cctcacaggt ttccagaatt acagt
                                                                       355
      <210> 438
      <211> 431
      <212> DNA
      <213> Homo sapien
      <400> 438
acagtaactt taactttaca tagagctgag ataaaaataa agctttctta caaattacat
                                                                       60
tttttttcca gtgaattact tttgcagtaa aaatagctgc tacataaatc cctcctgatc
                                                                      120
tctgaaaagg agttgcatat ttccaaaaat aatattctta ttttaatcac acagaagaac
                                                                      180
```

PCT/US99/30909

WO 00/37643

131

gtggagcaca ggaaggaaat ggctgggtgagttaaacta aaaaataaaa tccattttggtggaaaaca tatgccattt gtcaagaaaaaaggagaaa gcagaggcca gatataaggctcccaaatg t	gt gtataaactg aa atactgcttt	acttaaacgc atagctttta	atgcaaagaa ctttacaatt	240 300 360 420 431
<210> 439 <211> 170 <212> DNA <213> Homo sapien				
<pre><400> 439 actgtcataa aaaacagtgg agctctgta gtaactctag ttacacagaa actgtgacaaagaatcaaa gtcaactgac atctatgcaa</pre>	a aagtctatga	aactgattac		60 120 170
<210> 440 <211> 400 <212> DNA <213> Homo sapien				
<pre><400> 440 acgtaaaaag aacateette ecatette agtetteeag gatteeeag caggaatg ttgetteacg cacgeeteae ataceaga tcatetgtgt cectaceace tacaacag agaattaace atgatgggeg geegaggg ctettaggag agtgteagge tetaggeeg ggagtggtgg gatggaaace agaeggga</pre>	at ggeteeetgt et gaatgttgge ge eageaateta eg eetggageta ag tgteaceaga	ccctgtagct aggaggagtg cccgtgtgtg tttgggggct ggaggtcagt	ccaggagttc accaggtcgg tttgttggac tggagagaac	60 120 180 240 300 360 400
<210> 441 <211> 204 <212> DNA <213> Homo sapien				
<pre><400> 441 acctagttac ttcttaagat caggtgta atgacttgga atgtaagctg tcagggag ggtttcttca tattcctgct gttggaag aagcactgct gtgaaatgtg aagt</pre>	aa aatgttgtta	cacttttgct	aagatctggg	60 120 180 204
<210> 442 <211> 649 <212> DNA <213> Homo sapien				
<pre><400> 442 acatttaatt ttttacaaca ttttctcc aagtaaaaat caaaatagga aataagca catggtattt atgagtctcc aaactatt cttcattact tgggtgtaac tcgagaga tcatgatcag gggaaagtga tactcttc gaacttttcc tttattccta atatacag aatcaaattt aaatgaagta tccaggag tttagtctaa atttatgcct tgctcttc</pre>	ta gaaacagcctgg aaatttatttaa actaatttatca ctgactacaaga caaaccttgcta gcctaaagaa	attggcagtg caaccaaggt atcaatttac gtcattgcag cgacatctca tgagtgtaat	gttacacetg tctcttaagt agtttagtgg aggcagttta ctacctcaaa ctggatggat	60 120 180 240 300 360 420 480

```
acagatgcaa taatttctgt tccttgttcg gtgcagaata taatttatac ttcctgaaat
                                                                     540
caactttgtc tattcatgaa aatagctgct ttttatttgc ctttgtctca ctttgaatat
                                                                     600
atatgatcca caggitacag actiticcaa taactacati tcaactigi
                                                                     649
      <210> 443
      <211> 346
      <212> DNA
      <213> Homo sapien
      <400> 443
acgtgggatt gaaatgcaca tacatgtttt tgctaagagc acatacattt cattctcctc
                                                                      60
actitigatica taaccicage attigicagai aaccicagig agitaactica aagccittita
                                                                     120
ttatggaaag aactggcaca gttacatttg ccagtggcaa catccttaaa aattaataac
                                                                     180
tgatgggtca cggacagatt tttgacctag ttccttttc ttttagagca aaaagaactt
                                                                     240
300
gcaccctaaa cagccatttc cattttaata gttggatgcg gattgt
                                                                     346
      <210> 444
      <211> 425
      <212> DNA
      <213> Homo sapien
      <400> 444
accaatttcc ttttacagta aaggggcttt tectgttgct tgttgaaccg gttcccagct
                                                                      60
gcccattacc accaagccca aaagagtaaa ttcgtcctga tgaaggaaca aaagcagaag
                                                                     120
tgtgctgccg tccacaagca atctcagtga caatgcttcc cataagttca aaaactttcc
                                                                     180
ttgggtttat ttcatgactg gtagaattat ggcccaactg accataccct ccagetccaa
                                                                     240
aagtaaacac tccaccttcc ttggttagag cagcagtatg atcttctcca caacaaatat
                                                                     300
aaactatttt ctgagatctt agtgacttta gtaaattagg aacataccta tcattttcat
                                                                     360
cattaagacc tagctgacca aacttgttgc gtccccatcc aaagatagct ccagaaaggg
                                                                     420
tgagt
                                                                     425
      <210> 445
      <211> 210
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(210)
      <223> n = A, T, C \text{ or } G
      <400> 445
nactgtccca atataaaaca gtaattattt gacctttgca ctgtttgtct ggtccttttc
                                                                     60
agtttgattg catataaatg tggaacttga tagatctcta tatttttaat gcacttgtga
                                                                    120
taaactggca gcagggttag acattacttt caaagcttga ggtagaccga gtcagcatgc
                                                                    180
tagacaggct tctctctcta accaaaactg
                                                                    210
      <210> 446
      <211> 326
      <212> DNA
      <213> Homo sapien
      <400> 446
tcgaaagacc cctgtaaaag agcccaacag tgaaaatgta gatatcagca gtggaggagg
                                                                     60
```

PCT/US99/30909

```
cgtgacaggc tggaagagca aatgctgctg agcattctcc tgttccatca gttgccatcc
                                                                        120
actaccccqt tttctcttct tgctgcaaaa taaaccactc tgcccatttt taactctaaa
                                                                       180
caqatatttt tqtttctcat cttaactatc caagccacct attttatttg ttctttcatc
                                                                       240
tgtgactgct tgctgacttt atcataattt tcttcaaaca aaaaaatgta tagaaaaatc
                                                                       300
                                                                       326
atgtctgtga gttcattttt aaatgt
      <210> 447
      <211> 304
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(304)
      <223> n = A, T, C or G
      <400> 447
nentenaggt acatgetaga agtetgatgt ngtnngtaac acagaaacat acacagtett
                                                                        60
catattcaaa gtcttcacng ggatgtcgtt ctgtaatttc ctgcgtttgg gtctcttcca
                                                                       120
gaaacagett tagetteetg eteegaagge caaacacett ggetgettea tacagaagae
                                                                       180
cttggtgggt gagtccattc tgcccaagtg ggttttcaag caggagagtg cccactgtcc
                                                                       240
ccattaaaca ctcttgtggc tttgcattca ggagctgtag gttgatatac tgacaaygaa
                                                                       300
                                                                       304
gagt
      <210> 448
      <211> 203
      <212> DNA
      <213> Homo sapien
      <400> 448
acatgaaagc ggcaatgcgg taaaaagcga attcttaccc aaggtcagaa ttttttatta
                                                                        60
agegeatttt cattagttgg acaaacaace ttataaacee ttatgtcaaa ccatataatg
                                                                       120
tqaaqaatct ccatgggaga gattttttt cacccttcag aattatcttt ttcccctaag
                                                                       180
                                                                       203
accttcatat gaatcttcct tgt
      <210> 449
      <211> 481
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(481)
      <223> n = A, T, C \text{ or } G
      <400> 449
acttgttcta taatactctg atgtttcctt aaattcctga acaacattct gtttactaaa
                                                                        60
tttctttct tcctttattc acaccaaatt ccaccctata atagaagcta attattcaq
                                                                       120
aaagcttttt agtgatcatt tattactttg tgtttactag atattaattc taagatgaat
                                                                       180
tcctttagaa ttttagaaaa aattattcta gacaacaatc aaagtaaagg atacatccag
                                                                       240
cattgaaacc ataageegge aagteteeag gttaaaaggt ttgtateete eageaatgee
                                                                       300
agactgtgtc agacatctct gcaattcatc agcatctatc tgcccatcct gtccagctac
                                                                       360
agcagcaaaq taaccataca gcggatcctg agtttgtccg ggaaacgcag gccctccggg
                                                                       420
agececteca tactgeatet tgagttgaag tettatangt agaagetggt gateettaga
                                                                       480
                                                                       481
g
```

```
<210> 450
           <211> 296
           <212> DNA
           <213> Homo sapien
           <400> 450
     acatggttta atacaacaac aaaaaaattt aatcaagtga aacgtaataa actgaacaat
                                                                         60
     aaacactcaa aacattttcc attggaaaca tgtaaagaca atatgaggtt ttgttaccat
                                                                        120
     cttactgcaa ttttcttatg tgttactagt ctacataccc catgttttct gtaatcatgc
                                                                        180
     agatgtgaat ggaagtttga atgattaaat aaatgaaaag teegtttaet geagggaate
                                                                        240
     atttcacaag gcagccaaac cgggtttaga gaacaaaact attcaagaaa ttctcc
                                                                        296
           <210> 451
<212> DNA
           <213> Homo sapien
           <220>
           <221> misc_feature
           <222> (1)...(294)
           <223> n = A,T,C or G
           <400> 451
     acatgntcca aggcacgcgn ctgtgaactt cctctgagtg aaggcatccc ctccagcacc
                                                                        60
     tttcagcctg ctagttagga cgacccgccg ccaccctcca ggacctccag ccctgcactg
                                                                        120
     cettteetet ettttaaata attetteatt gagttetaat atgtaaaaaa aaagtttaet
                                                                        180
     gtaaagtttg caaataanga aattttttt aaaagtcctc agtaatctta ccagtaacaa . 240
     ttgttatggg cacatutgct tttggaagat ttcttttgta tgcatgggat aagt
                                                                        294
           <210> 452
           <211> 129
           <212> DNA
           <213> Homo sapien
           <400> 452
     acttttagat cacaaatttg cctttaagta acacataata cacttaaggc agatttgcct
                                                                        60
     tacaggtggc ctcagcttct aaacaccact acactgcttt atataaaaaa caaaaatcac
                                                                        120
     atagaagag
                                                                        129
          <210> 453
          <211> 151
           <212> DNA
          <213> Homo sapien
          <220>
          <221> misc_feature
          <222> (1)...(151)
          <223> n = A, T, C \text{ or } G
          <400> 453
     actctcaann tgtatttagg tgccaacaca tttaggatca ttgngnnttc tcagtgaatt
                                                                        60
     gaccttttta tgagaataaa atgtctattt ctgaaatgtc cctatttctg gaaatgttcc
                                                                        120
     ttatactaaa gtccaacttg tgtggattan t
                                                                        151
```

```
<210> 454
       <211> 119
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(119)
      <223> n = A, T, C \text{ or } G
      <400> 454
tgctgatgna gcatgctttt taaatccttt aaaaacactc accatataaa cttgcatttg
                                                                        60
agettgtgtg ttettttgtt aatgtgtaga gtteteettt etegaaattg eeagtgtgt
                                                                        119
      <210> 455
      <211> 515
      <212> DNA
      <213> Homo sapien
      <400> 455
accttataaa gttccttttc atccttctct gtcttcaact gacattcaag ttgttctctt
                                                                         60
tratgttgtg cottottgag trtggcottt aaactgtota attoggttto tttttcaart
                                                                        120
gctttatgtg ttactyacac aatatcttcc tcaagctgat gggctttgga tgtagcatca
                                                                        180
ctgaacctct tcttaaactc ttcattttcc atttttaagc tttgtgttac ttcagtaaga
                                                                        240
cccttttgtt ctgcttgcag ttggtcacat ctttctttct catggttaag ttctctttcc
                                                                        300
atteteceaa ettgtteteg aagttgtget gtttetttt ceagaaegge aattaaettt
                                                                        360
aacagttett ettittetit catggtttte teaattttea aeteaagaag geetgetttt
                                                                        420
gtggtcacca ctaacatgtc agaatttcct tcatcttcca tagtaagcag ctcttcaact
                                                                        480
ggagaagaag ctcgaaactg gaaaggtgta cctgc
                                                                        515
      <210> 456
      <211> 350
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(350)
      <223> n = A, T, C or G
      <400> 456
actcccctcc ccaaatagaa acctcaaaga ctgatccatt tcccctaggg cctgggccag
                                                                      . 60
gagtagctca ctgctcactg ctgaggagaa aggcacaaga tataatgtca taagagcagg
                                                                       120
acagtggctc agcctacaga gttccctata ggggaaagaa ggcaggaaat aggcgcaggg
                                                                       180
tctggtcctg tccctgcacc accctgagca gctagtcttg ggaagggatt acaggccctg
                                                                       240
ggccataggc tgctcgccat tctgctttcc tatcctgttt ctctccctgt gctgctccct
                                                                       300
tttagccagn gctgagaaat gttcancacc tgaggcaaaa ctgccatagt
                                                                       350
      <210> 457
      <211> 293
      <212> DNA
      <213> Homo sapien
      <400> 457
gcagggccaa cagtcacage agccetgace agageattee tggageteaa geteetetae
                                                                        60
```

136

```
aaagaggtgg acagagaaga cagcagagac catgggaccc ccctcagccc ctccctgcag
                                                                       120
attqcatqtc ccctggaagg aggtcctgct cacagcctca cttctaacct tctggaaccc
                                                                       180
acccaccact gccaagetca ctattgaatc cacgccattc aatgtcgcag aggggaagga
                                                                       240
gqttcttcta ctcqcccaca acctqcccca gaatcqtatt ggttacagct ggt
                                                                       293
      <210> 458
      <211> 500
      <212> DNA
      <213> Homo sapien
      <400> 458
actagactcc agattaccct ttcttaataa atatctcagg gtaaggaaag aaagaaactg
                                                                        60
tatagatata tttaaaatag agaatacttt ccaagcaata catgatgcct ttcctaaaag
                                                                       120
actictaaaag aaaaagatti tigtaacticti tittagcacc aaattattigt tiaticttiget
                                                                       180
ggatatttta tatgaacagt gttaatttag atgcactaaa gcaaaggtag gcaaactaca
                                                                       240
                                                                       300
accatqagte aaacatggce acacccatte atttgctatt gtctaagetg gttttgcact
acaactgcag agttgaatag atgcagcaga tectttacag aaaaagtttt etgacetcaa
                                                                       360
ttctaaagta attgtagtag ggagctggag gactttcttt ccctttatgg taattttttg
                                                                       420
agctacaaaa agagccttgc agaaatgggt gaagggatta atcttttaaa aataaatgct
                                                                       480
atatattagg aaaataaaaa
                                                                       500
      <210> 459
      <211> 394
      <212> DNA
      <213> Homo sapien
      <400> 459
ggtgaaaaga cttgattttt tgaaaggatt gtttatcaaa cacaattcta atctcttctc
                                                                        60
ttatgtattt ttgtgcacta ggcgcagttg tgtagcagtt gagtaatgct ggttagctgt
                                                                       120
taaggtggcg tgttgcagtg cagagtgctt ggctgtttcc tgttttctcc cgattgctcc
                                                                       180
tqtqtaaaqa tgccttgtcg tgcagaaaca aatggctgtc cagtitaita aaatgcctga
                                                                       240
caactqcact tccagtcacc cgggccttgc atataaataa cggagcatac agtgagcaca
                                                                       300
totagotgat gataaataca cottttttto cotottocco otaaaaatgg taaatotgat
                                                                       360
                                                                       394
catatctaca tgtatgaact taacatggaa aatg
      <210> 460
      <211> 279
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(279)
      <223> n = A,T,C or G
      <400> 460
actneegatt gaageeeca ttegtataat aattacatea caagaegtet tgeacteatg
                                                                        60
agctgtcccc acattaggct taaaaacaga tgcaattccc ggacgtctaa accaaaccac
                                                                       120
tttcaccgct acacgaccgg gggtatacta cggtcaatgc tctgaaatct gtggagcaaa
                                                                      .180.
ccacagtttc atgcccatcg tcctagaatt aattccccta aaaatctttg aaatagggcc
                                                                       240
cgtatttacc ctatagcacc ccctctagag caaaaaaaa
                                                                       279
      <210> 461
      <211> 278
      <212> DNA
```

60

137

<213> Homo sapien

```
<400> 461
 tttggacact aggaaaaaac cttgtagaga gagtaaaaaa tttaacaccc atagtaggcc
 taaaagcagc caccaattaa gaaagcgttc aagctcaaca cccactacct aaaaaatccc
                                                                       120
 aaacatataa ctgaactcct cacacccaat tggaccaatc tatcacccta tagaagaact
                                                                        180
 aatgttagta taaagtaaca tgaaaacatt ctcctccgca taagcctgcg tcagattaaa
                                                                        240
 acactggact gacaattaac agccaatatc tacaatca
                                                                        278
<210> 462
<211> 556
<212> DNA
<213> Homo sapiens
<400> 462
aacgtccaag ggggccacat cgatgatggg caggcgggag gtcttggtgg ttttgtattc 60
aatcactgtc ttgccccagg ctccggtgtg actcgtgcag ccatcgacag tgacgctgta 120
ggtgaagegg ctgttgccct cggcgcggat ctcgatctcg ttggagccct ggaggagcag 180
ggccttcttg aggttgccag tctgctggtc catgtaggcc acgctgttct tgcagtggta 240
ggtgatgttc tgggaggcct cggtggacat caggcgcagg aaggtcagct ggatggccac 300
ateggeaggg teggageest ggeegeeata etegaactgg aatecategg teatgetete 360
geogaaceeg acatgeetet tgteettggg gttettgetg atgtaceagt tettetggge 420
cacactgggc tgagtggggt acacgcaggt ctcaccagtc tccatgttgc agaagacttt 480
gatggcatcc aggftgcagc cttggttggg gtcaatccag tactctccac tcttccagtc 540
agagtggcac atcttg
                                                                  556
<210> 463
<211> 659
<212> DNA
<213> Homo sapiens
<400> 463
cacactgtgc ccttccagtt gctggcccgg tacaaaggcc tgaacctcac cgaggatacc 60.
tacaagcccc ggatttacac ctcgcccacc tggagtgcct ttgtgacaga cagttcctgg 120
agtgcacgga agtcacaact ggtctatcag tccagacggg ggcctttggt caaatattct 180
totgattact tocaagoooc ototgactac agatactaco cotaccagto ottocagact 240
ccacaacacc ccagcttcct cttccaggac aagagggtgt cctggtccct ggtctacctc 300
cccaccatcc agagetgetg gaactaegge tteteetget ceteggaega geteeetgte 360
ctgggcctca ccaagtctgg cggctcagat cgcaccattg cctacgaaaa caaagccctg 420
atgetetgeg aagggetett egtgyeagae gteacegatt tegagggetg gaaggetgeg 480
attoccagtg coetggacac caacageteg aagageacet ceteetteec etgeceggea 540
gggcactica acggcticeg cacggtcate egecectict acctgaccaa etecteaggt 600
gtggactaga cggcgtggcc caagggtggt gagaaccgga gaaccccagg acgccctca 659
<210> 464
<211> 695
<212> DNA
<213> Homo sapiens
<400> 464
accttcattt gaccccatca gcttcagggc cttctttaca tttccactgg cctgatccat 60
gtatgcaatg ctatttttgc agtgatatgt gatgttctgg gaagctcggc tggagagaag 120
tcgaaggaat gccagctgca catcaaggac atcttcagga agttcaggat tgccgtagct 180
aaactgaaaa ccaccatcca tggactctcc aaaccaaacg tgtttcttct cagcactaga 240
atotgtocac cagtgtttoc gtggaacatt caaaggattg gcacttatgc atgtttcccc 300
```

```
agtttccata ttacagaata ccttgatagc atccaatttg catccttggt tagggtcaac 360
ccagtattct ccactcttga gttcaggatg gcagaatttc aggtctctgc agtttctagc 420
ggggttttta cgagaaccat caggactaat gaggctttct atttgtccat taacagactt 480
gagtgaagtc ataatctcat cggtgttgat tttgaaatcc attggttcat ctccataata 540
cggggcaaaa ccgccagctt tttcacctcc aatcccagca atggcagcgg ctccaacacc 600
accacagcaa ggaccagggg caccaggagg tccaggaggg cctggttgcc ctgggtggcc 660
tggggagccc tcagatcctc tttcacctct gttac
<210> 465
<211> 73
<212> DNA
<213> Homo sapiens
<400> 465
caggiccaga geteccaggi ticcaggity cagiccetee agreecagag eteccagggit 60
ttcggtttcc agt
<210> 466
<211> 507
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(507)
<223> n = A, T, C or G
<400> 466
aagcatattg ctatacaaga ctttaaagac ttcataaaag ccaaacttgc agagtccctg 120
catggagtag ccaaggaaag teggageeea teetttagee aaaccaegaa caccateete 180
tttaagtgta actgagaatc cgttaaatat gcccttgtac ttttgggggt ccacctgcat 240
acggcatttc actaaatcca ggggaaccac agcagtgtgt gtcagaccac aacttaagac 300
cccaccaaag ccacacagtg cataatactt cgcggagcca aattcacaac tgtactcttc 360
cacggcggcg gctgccaggt tgcgagggcg gcggggctgg cccgtgggcc ctggggagct 420
gctgcggagg tccccgagac catcgtgcac canctgcaga tgtggcgtgt tgaaggggtt 480
cgcccgcgcc aggtgcgcca cggacga
                                                                507
<210> 467
<211> 183
<212> DNA
<213> Homo sapiens
<400> 467
cctcatgagc taccgggcca gctctgtact gaggctcacc gtctttgtag gggcctacac 60
cttctgagga gcaggaggga gccaccetce etgcagetae cetagetgag gageetgttg 120
tgaggggcag aatgagaaag gcaataaagg gagaaagaaa aaaaaaaaa aaaagggcgg 180
ccg
                                                                183
<210> 468
<211> 129
<212> DNA
<213> Homo sapiens
<220>
```

```
<221> misc_feature
<222> (1)...(129)
<223> n = A,T,C or G
<400> 468
gcggccgcgt cgaccggcgc cgtcgggcnc cgggccgggc catggagctg tggacgtgtc 60
tggccgcggc gctgctgttg ntgntgctgn tggtgcagtt gagccgcncn gccgagttct 120
<210> 469
<211> 243
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(243)
<223> n = A,T,C or G
<400> 469
gcggccgcgt cgacnggcca tggagactgt ggcacagtag actgtagtgt gaggctcgcg 60
ggggcagtgg ccatggaggc cgtgctgaac gagctggtgt ctgtggagga cctgctgaag 120
tttgaaaaga aatttcagtc tgagaaggca gcaggctcgg tgtccaagag cacgcagttt 180
gagtacgcct ggtgcctggt gcggagcaag tacaatgatg acatccgtaa aggcatcgtg 240
                                                                    243
<210> 470
<211> 452
<212> DNA
<213> Homo sapiens
<400> 470
cctcaagtac gtccggcctg gtggtgggtt cgagcccaac ttcatgctct tcgagaagtg 60
cgaggtgaac ggtgcggggg cgcaccctct cttcgccttc ctgcgggagg ccctgccagc 120
teccagegae gaegeeaceg egettatgae egaeceeaag eteateacet ggteteeggt 180
gtgtcgcaac gatgttgcct ggaactttga gaagttcctg gtgggccctg acggtgtgcc 240
cctacgcagg tacagccgcc gcttccagac cattgacatc gagcctgaca tcgaagccct 300
gctgtctcaa gggctcagct gtgcctaggg cgccctcct accccggctg cttggcagtt 360
gcagtgctgc tgtctcgggg gggttttcat ctatgagggt gtttcctcta aacctacgag 420
ggaggaacac ctgatcttac agaaaatacc ac
<210> 471
<211> 168
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(168)
\langle 223 \rangle n = A,T,C or G
<400> 471
cttctccgct ccttctanga tctccgcctg gttcggnccg cctgcctcca ctcctgcctc 60
taccatgtcc atcagggtga cccagaagtc ctacaaggtg tccacctctg gcccccgggc 120
cttcagcagc cgctcctaca cgagtgggcc cggttcccgc atcagctc
```

```
<210> 472
        <211> 479
        <212> DNA
        <213> Homo sapiens
        <220>
        <221> misc_feature
        <222> (1)...(479)
        <223> n = A, T, C or G
        <400> 472
        gccaggcgtc cototgtotg cocactoagt ggcaacaccc gggagctggt ttgtcctttg 60
        tggagcctca ncagttccct ctttcanaac tcactgccaa gagccctgaa caggagccac 120
cargeagrac ricagorica traagaccar gargareer treaattree teaterret 180
        gngtggcgca gccctgttgg cagcgggcat ctgggtgnca atcgatgggg catcctttct 240
        gaagatette gggeeactgt egteeactge catgeagttt gteaaegngg getaetteet 300
        categoagee ggegttgtgg tntttgetet tggttteetg ggetgetatg gtgetaanae 360
        tgagagcaag tgtgccctcg tgacgntctt cttcatcctc ctcctcntct tcattgctga 420
        ggntgcagnt gctgaggtcc gccttggtgt acaccacaat ggctgagccc ttnctgacn 479
        <210> 473
        <211> 69
        <212> DNA
        <213> Homo sapiens
        <400> 473
        gagcgatgga gcgtgggtag ggagggtcca cagtgtccac tcgccgtgtg cgaaggttga 60
        ctcggtagt
                                                                          69
        <210> 474
        <21.1> 155
        <212> DNA
        <213> Homo sapiens
        <400> 474
        geogecactg cogggagage togatggget tetectgege geogeceggt gtetggeega 60
        gtccagagag ccgcggcgcc tcgttccgag gagccatcgc cgaagcccga ggccgggtcc 120
        cgggttgggg actgcagggg aaggcagcgg tggcg
                                                                          155
        <21.0> 475
        <211> 282
        <212> DNA
        <213> Homo sapiens
       <400> 475
       ggcttcgacg ttggccctgt ctgcttcctg taaactccct ccatcccaac ctggctccct 60
       cccacccaac caacttteec cccaaccegg aaacagacaa gcaacccaaa ctgaaccecc 120
       tcaaaagcca aaaaatggga gacaatttca catggacttt ggaaaatatt tttttccttt 180
       gcattcatct ctcaaactta gtttttatct ttgaccaacc gaacatgacc aaaaaccaaa 240
       agtgcattca accttaccaa aaaaaaaaaa aaagggcggc cg
                                                                         282
       <210> 476
       <211> 434
       <212> DNA
```

```
<213> Homo sapiens
<400> 476
ctccaggaca gcgtccagct tggtgtcgtt gaagacgaag tggagcggat ggttgtagaa 60
acgagtgatg gtgctgagcg gcgtgcagtc ttcgggatcc acgaaggcca agtccttgag 120
gtagagcatg tccacgatgt tggagcgctc ctcctcgtac accgggatgc gcgtgtggcc 180
gctctgcatg atgctggcca ggacgccgaa gtccagcacg gtgctggcgt ccagcatgaa 240
gcagtcttcg aggggcgtga gcacgtcctc cacggtccgg cagcgcagca cgcccttgct 300
gagategetg taggggtege egeegeegeg egeeagetee ageaceeget eeegeageeg 360
cccgggccgc gccgccagct ccagcagctg ccccacgggc agcgcgacgg gcagagtgag 420
caggacggcc aggc
                                                                   434
<210> 477
<211> 31.4
<212> DNA
<213> Homo sapiens
<400> 477
ggcgggcgct agctggctcc gggcagctcg gccttggggg cttcggggcc ccgagacgcg 60
gggcgtatga gtggggcgtg cgctccacgc ggaagtcgga gcctcctccc ctggataggg 120
tgtacgagat ccctggactg gagcccatca cctttgcggg gaagatgcac ttcgtgccct 180
ggctggcgcg gccgatcttt ccgccctggg accgcggcta caaggaccca aggttctacc 240
getogeecc tetteacgag cateogetgt acaaagacca ggeetgetat atettteacc 300
accettgccg cctt
                                                                   314
<210> 478
<211> 317
<212> DNA
<213> Homo sapiens
<400> 478
aacagagtga tcattccagt taagcggggc gaagagaata cagactatgt gaacgcatcc 60
tttattgatg gctaccggca gaaggactcc tatatcgcca gccagggccc tcttctccac 120
acaattgagg acttctggcg aatgatctgg gagtggaaat cctgctctat cgtgatgcta 180
acagaactgg aggagagagg ccaggagaag tgtgcccagt actggccatc tgatggactg 240
gtgtcctatg gagatattac agtggaactg aagaaggagg aggaatgtga gagctacacc 300
gtccgagacc tcctggt
                                                                   317
<210> 479
<211> 171
<212> DNA
<213> Homo sapiens
<400> 479
aggtgctttg ctagatgctg tgacaggtat gccaccaaca ctgctcacag cctttctgag 60
gacaccagtg aaagaagcca cagctcttct tggcgtattt atactcactg agtcttaact 120
tttcaccagg ggtgctcacc tctgccccta ttgggagagg tcataaaatg t
<210> 480
<211> 65
<212> DNA
<213> Homo sapiens
<400> 480
cccccagtgg aaggeteeca ccctggtaga tgaacageec ctggagaact acctggatat 60
```

142

```
65
ggagt
<210> 481
<211> 207
<212> DNA
<213> Homo sapiens
<400> 481
cacagogtgc totgoggggt cactoccact ttgttagtga tgtggttatc toctcagatg 60
gccagtttgc cctctcaggc tcctgggatg gaaccctgcg cctctgggat ctcacaacgg 120
gcaccaccac gaggcgattt gtgggccata ccaaggatgt gctgagtgtg gccttctcct 180
ctgacaaccg gcagattgtc tctggat
<210> 482
<211> 319
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(319)
\langle 223 \rangle n = A,T,C or G
<400> 482
cacactgtgc cettecagtt getggcccgg tacaaaggcc tgaacctcac cgaggatacc 60
tacaageece ggatttacae etegeecaee tggagtgeet ttgtgacaga cagtteetgg 120
agtgcacgga agtcacaact ggtctatcag tccagacggg ggcctttggt caaatattct 180
totgattact tocaagooo ctotgactac agatactace cotaccagtg ottocaaact 240
geacaacace enagettnet ettecagnac aagagggtgt cetggteest ggeetacete 300
                                                                    319
cccaccatcc agagetget
<210> 483
<211> 233
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(279)
<223> n = A,T,C or G
<400> 483
acaggeccag tggegectag cetteagetg etgggetete eegageetge ettageccat 60
acaaccactt gatcacgcgg gcattgcgct ccaccaccga cacgccatag ggaacgcgct 120
cccgggcccg ctcctcaaca gtcaccgagc tgcggcggga gcagccccct tcagagctgc 180
ccggcccagc actgggccct gccagggaca cnatatccga gctggcccgt gcc
                                                                   233
<210> 484
<211> 194
<212> DNA
<213> Homo sapiens
<400> 484
agagecettg etggggggtg cetgggagat ggggtaagaa gagettteat ttgtetggta 60
gatagatagc atgtaagggg gtggttgtcc caggaggcag ctgctgacag gtttgctaca 120
```

cacageceeg tgtgeceetg		cctgggtgct	cattcagaga	ggggctatca	tctgggagcc	180 194
<210> 485 <211> 67 <212> DNA <213> Homo	sapiens					
<400> 485 tccatatcca gggaagt	ggtagttctc	caggggctgt	tcatctacca	gggtgggagc	ctcccactgg	60 67
<210> 486 <211> 70 <212> DNA <213> Homo	sapiens					
<400> 486 taccgagtca atcgctcagt	accttcgcac	acggcgagtg	gacactgtgg	accctcccta	cccacgct.cc	60 70

THIS PAGE BLANK (USPTO)